SCIENCE

19 June 1959

Volume 129, Number 3361

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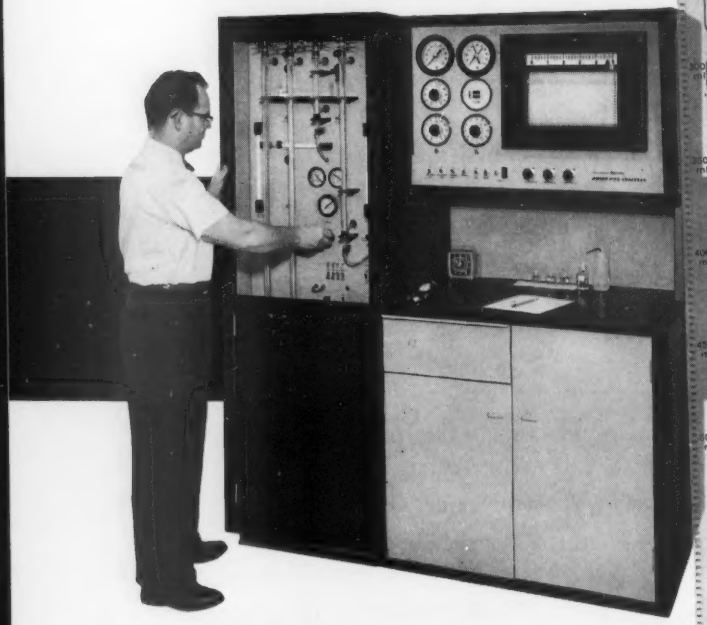

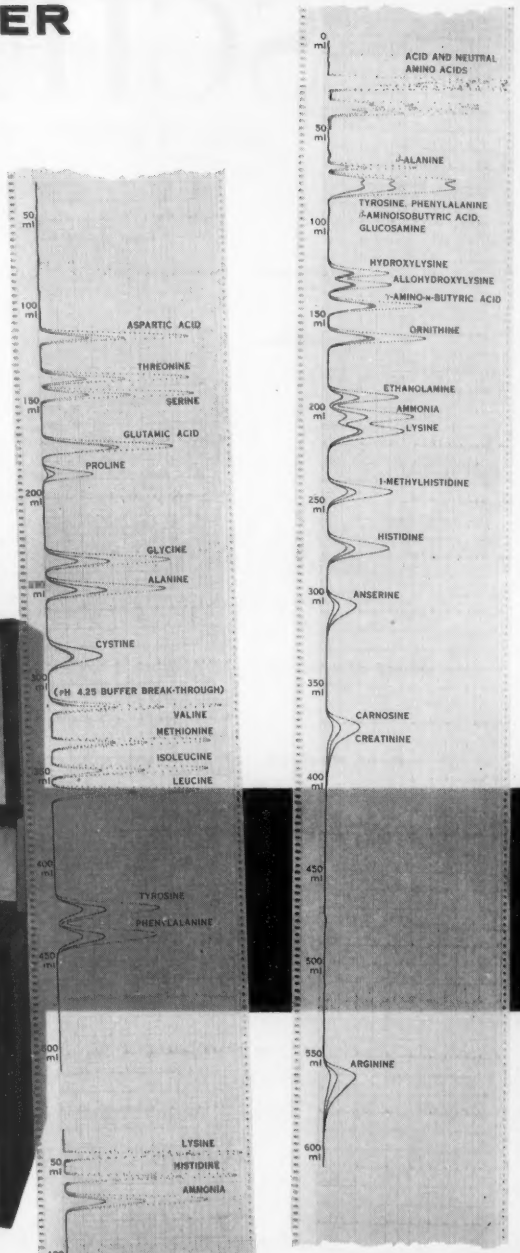

Reference: *D. H. Spackman, W. H. Stein, and S. Moore, "Automatic Recording Apparatus for use in the Chromatography of Amino Acids", Anal. Chem., 30, 1190-1206, 1958.*

Chart at left is analysis of amino acids found in protein hydrolysates: top run on 150-cm column at 50°C and pH 3.25 buffer, with changeover to pH 4.25 buffer at 6 hours; lower run on 15-cm column at 50°C and pH 5.28 buffer

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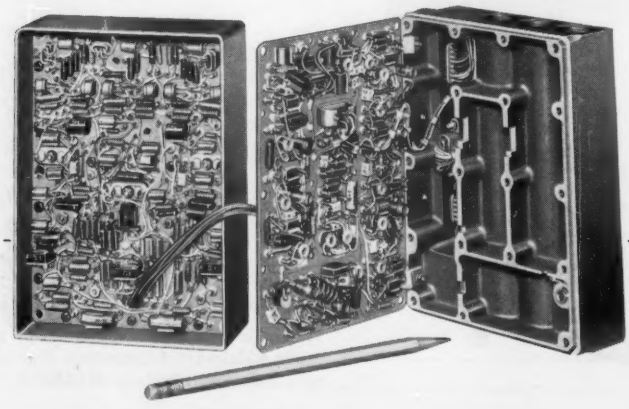

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19 June 1959, Volume 129, Number 3364

SCIENCE

SCIENCE, which is now combined with THE SCIENTIFIC MONTHLY, is published each Friday by the American Association for the Advancement of Science at Business Press, Lancaster, Pa. The joint journal is published in the SCIENCE format. Entered at the Lancaster, Pa., Post Office as second class matter under the Act of 3 March 1879. SCIENCE is indexed in the *Reader's Guide to Periodical Literature*.

Editorial and personnel-placement correspondence should be addressed to SCIENCE, 1515 Massachusetts Ave., NW, Washington 5, D.C. Manuscripts should be typed with double spacing and submitted in duplicate. The AAAS assumes no responsibility for the safety of manuscripts or for the opinions expressed by contributors. For detailed suggestions on the preparation of manuscripts, book reviews, and illustrations, see *Science* 125, 16 (4 Jan. 1957).

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Unsettling Side to Settling Technical Issues

Several recent disputes between Congress and the Administration over appropriations for research and weapons pose again the question of how successful our government is at bringing objective judgment to bear on technical issues. One dispute between Congress and the Administration is over the direction of the nuclear-powered aircraft program. Some members of the Joint Committee on Atomic Energy want funds increased and a big effort made now to get a plane in the air, while the Administration wants to limit the program to further research on the power plant. The word *limited* is perhaps not quite right, for, although apparently no power plant has yet been demonstrated, almost a billion dollars has been spent on the project in the past 13 years.

Members of the Congressional committee have argued for early flight, that is, flight in the next four or five years, on the grounds that this effort would answer technical questions that the designers of later models would also have to face. And committee members have emphasized the propaganda value of having a nuclear-powered aircraft before the Soviets do. The Administration's position is that to begin construction of a fuselage and power plant before further research on the power plant would result in a plane of such poor performance that it would be nothing to boast about and would be of no military use.

Another dispute between Congress and the Administration involving technical matters is over the relative merits of the Air Force's Bomarc missile, the Army's Nike-Hercules, and the Army's Nike-Zeus. The Bomarc is designed for area defense, while the Nike-Hercules is designed for point, or last-ditch, defense. Both weapons are for use only against piloted aircraft, while the Nike-Zeus is for defense against ballistic missiles. Besides differing in use, the weapons also differ in their state of development, with the Nike-Hercules the most proven weapon. In sending the defense money bill to the Senate, the House cut drastically the Administration's recommendation for the Bomarc program, left the Nike-Hercules program unchanged, and added substantially to the Nike-Zeus program.

How do Congress and the Administration compare in their efforts at deciding technical issues? Many observers find that when Congress attempts to decide technical matters, it is more likely to do so on the basis of political and financial factors than on scientific or military ones. Indeed, President Eisenhower made this point recently when replying to a reporter's question concerning his having spoken sharply to several Senators about what the President was quoted as calling a "munitions lobby." Of course, Congress can fill important functions. By challenging appropriations, for example, it can force the Administration to make decisions that the Administration has so far failed to make. Congressional action on the various missile programs resulted in the Pentagon's deciding questions of air defense, including such matters as the proper mix of the weapons, in its efforts to push its program in the Senate.

When the Administration does decide technical matters, so many observers find, it does have a good chance of deciding them on an objective basis. The Administration's decision in this year's budget message to support further research on the power plant before attempting to fly a nuclear-powered aircraft is based in part on the judgment of the President's Science Advisory Committee. However, the Administration can also be subjected to pressure from political groups, the armed services, and companies in the defense business. At the insistence of the Joint Committee on Atomic Energy, the nuclear-powered aircraft program has again been brought under review. It will be instructive to see whether the Administration's position changes, and, if so, what its reasons are.—J.T.

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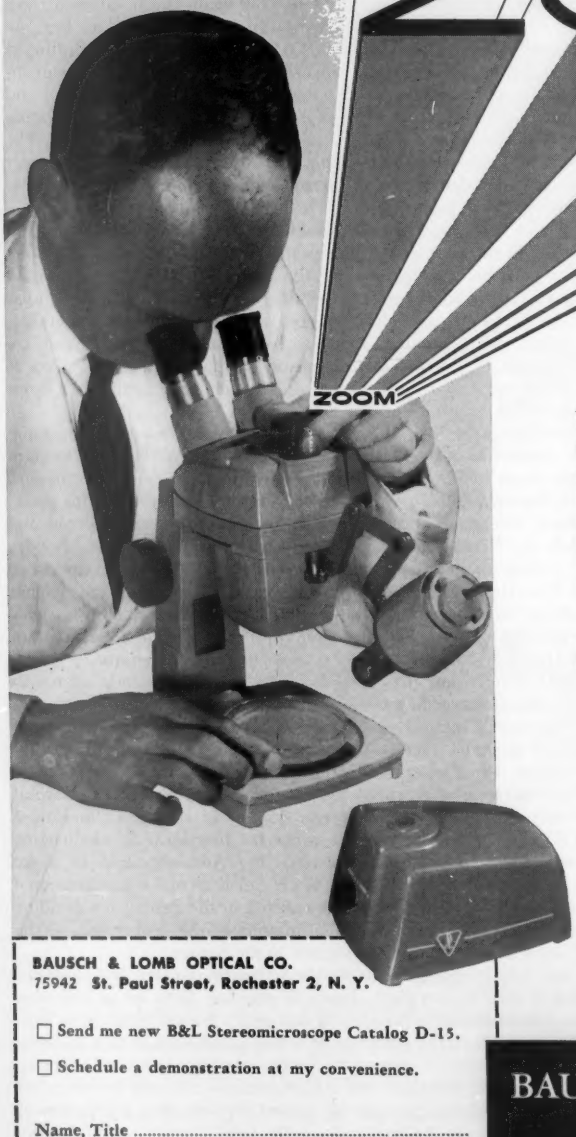

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CURRENT PROBLEMS IN RESEARCH

Immunological Specificity

Unique combinations of selected natural globulins provide an alternative to the classical concept.

David W. Talmage

The elucidation at a molecular level of the nature of specific biological interactions constitutes one of the most important and challenging problems of biology today. Specificity was defined by Landsteiner (*1*, p. 6) as the "disproportional action of a number of similar agents on a variety of related substrata." Specificity is a property of a wide range of biological agents such as antibodies, antibiotics, toxins, viruses, enzymes, genetic material, and plant agglutinins. Of these, only antibodies have the property that their production by the host can be stimulated by the injection of an almost unlimited range of substances. Furthermore, an antiserum reacts specifically with the antigen which stimulated its production, thereby providing a powerful tool for the detection and identification of biological materials.

It is probable that by the use of appropriate antisera any of the millions of species of plants, animals, and microorganisms can be distinguished from one another. Landsteiner, to whose name and work the subject of immunological specificity is most closely attached, extended the demonstration of the range of this specificity to a wide variety of simple synthetic compounds. It would thus appear that the number of substances which may be distinguished and identified is nearly infinite if it includes all substances which have been and are yet to be synthesized. This is, indeed, distinctive behavior.

In view of the uniqueness of antibody specificity, it is not surprising that immunologists have always considered that the relationship of an antibody to its antigen is something special. The term *anti-egg albumin* which designates an antibody to egg albumin carries with it the concept of special formation along with the concept of specificity. Whereas other types of specific interactions could be attributed to chance structural complementariness between independently fabricated molecules, in the case of antibodies this idea was generally rejected because of the infinitely large number of different molecules thought to be required. Because of these considerations, Landsteiner stated, "there remains hardly any other conclusion than . . . to assume that under the influence of antigens the formation of certain globulins (and perhaps normal antibodies) is modified in such a manner that the resulting globulins are closely adapted to the immunizing substance" (*1*, p. 148). This concept of a special relationship between antigen and antibody has been a cornerstone of immunological thinking for half a century. Widely accepted before Landsteiner's important work, it has not been seriously challenged since.

The classical line of reasoning which leads to the conclusion quoted above may be divided into the following steps.

1) In many vertebrates, the response to the injection of any one of a very large number of substances is the formation of antibodies capable of identifying the substance injected and thus distinguishing it from all other substances.

2) The antibodies so formed must be different and unique for each of the many substances to which a distinctive response can be made.

3) An animal could not possess of itself the information necessary to synthesize all of the different types of antibodies it is capable of forming in response to the varied environmental stimuli.

4) Antibodies must represent a unique modification in the synthesis of natural protein for which information is supplied by the antigen injected.

Weaknesses

While it is understandable that this line of reasoning seemed inescapable only 20 years ago, several weaknesses have developed in the argument as the result of the progress of knowledge in immunology and related fields of biology.

An increasing awareness of the diversity of antibodies in a single antiserum has emphasized the distinction between an antiserum and the antibodies it contains (for reviews, see *2–4*). Although it is necessary that a different antiserum be formed for each antigen that may be distinguished, it is possible that the large number of different antisera contain a much smaller number of different antibodies in different combinations. For example, a system consisting of only five different antibodies, A, B, C, D, and E, could distinguish nine antigens which reacted with three of the five in different combinations: ABC, ABD, ABE, ACD, ACE, BCD, BCE, BDE, and CDE. The distinguishing ability of antisera is similar to that present in this simplified system, for the injected antigen is distinguished largely by the fact that it reacts with the maximum number of anti-

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bodies. The concept that a different antibody is made for each antigen is inherent in the conclusion of step 4 in the classical line of reasoning given above. Its insertion in step 2 is an assumption which makes the final conclusion almost inevitable.

An almost unlimited number of different antibodies is not only unnecessary to explain immunological specificity, but may be an impossible assumption. The finding that the combining site on the antibody molecule is relatively small (*5*) has raised the question of whether it is possible to construct a unique antibody molecule for each of the almost infinite number of antigens. This question is particularly relevant if it is considered that not one but a whole family of different antibody molecules with different combining constants is made in response to a single antigenic determinant, and that all of these molecules appear nearly identical to the other gamma globulins of that animal in physicochemical properties, in amino acid composition and sequence, and in antigenic properties.

Another problem which has raised doubts concerning the uniqueness of antibodies is the difficulty in defining the term. Antibodies are so diverse in their physical properties and in their reactions with antigens and blend so gradually into obviously nonantibody substances that any definition is necessarily arbitrary (*6*).

While the preceding considerations cast doubt on the uniqueness of the relationship between an antibody and its antigen, other developments have brought into question the concept that antibodies are necessarily modifications of a normal protein. The analogy of induced enzyme synthesis in bacteria has demonstrated that a substance may appear where nothing was previously detectable without necessarily implying the production of a new substance (*7*). The induction by environmental stimuli of an increased production of naturally occurring animal proteins such as properdin (*8*) or ferritin (*9*) has indicated the existence of induced protein synthesis in animals. The relatively large number of genetically determined enzymes which can be synthesized by a bacterium has increased the estimates of the number of different natural proteins which can be synthesized by a vertebrate. It has been estimated that there is enough deoxyribonucleic acid (DNA) in a single human cell to encode 1000 large textbooks (*10*).

Perhaps the most compelling reasons for questioning the concept that antibodies are globulins modified by antigens are the recent observations relative to immunological tolerance—that is, the finding that except under unusual circumstances an adult animal does not synthesize antibodies to his own substances which are antigenic to other individuals. The mechanism of this obviously advantageous characteristic is not known, nor it is known to what extent, if any, this is due to restrictions imposed by heredity. That it is at least partially acquired during development might be deduced from the fact that with the exception of highly inbred animals, an individual can make antibodies against the antigens of both his parents. The most striking experimental evidence that immunological tolerance can be acquired is its establishment by the injection of foreign antigens during an immunologically unresponsive period—for example, during the fetal or immediate newborn periods (*11*), or after whole body x-radiation (*12*).

If after the initial injection into a newborn animal the concentration of antigen is maintained by repeated injections or by use of a viable, replicating cellular antigen, tolerance may last indefinitely. If the concentration of antigen falls below a critical level for a short period, subsequent injection of the same antigen may lead to antibody production (*13*). Unlike the accelerated secondary antibody response to an antigen, tolerance to an antigen in the absence of that antigen is short-lived. Probably related to immune tolerance are recent observations which indicate that antibody-producing cells are highly specialized. In a study of 456 single lymph node cells from a rabbit immunized to two different salmonellae, Nossal and Lederberg (*14*) found 33 cells that synthesized immobilizing antibody to one organism, 29 cells that synthesized antibody to the other, and no cells that synthesized antibody to both. This confirms a similar conclusion that Coons (*15*) drew from studies of doubly immunized animals with fluorescein-labeled antibody markers.

It is impossible to conclude from both of these experiments that cells do not make more than one type of protein, but only that the number of types any cell can make is greatly restricted compared with the capacity of the organism as a whole. In this sense they are highly specialized. There is a strong implication in other work that the immediate precursors of antibody-producing cells are also highly specialized. When cells from immunized animals are transferred to normal, tolerant, or x-radiated recipients, a prompt anamnestic response is obtained from an injection of the original antigen (*16*), but not from an injection of another antigen. The difference between the tolerant and sensitized animals would seem to lie in the possession by the latter of a large number of differentiated precursors of antibody-producing cells. Therefore, in some way the process of immune tolerance must be related to the process of cell differentiation and replication.

Role of Antigen in Cell Differentiation

The key issue relevant to this discussion is the role of antigen in the differentiation of antibody-forming cells. Although antigen-induced differentiation might seem an obvious analogy to substrate-induced permease synthesis in bacteria (*17*), differences arise because specific capabilities in the latter phenomenon are strictly inherited and are not associated with anything analogous to acquired immune tolerance. In order to explain acquired immune tolerance in animals, it is necessary to postulate a recognition system capable of distinguishing between the antigen and the tolerated substance (*18*). If one chooses the hypothesis that the antigen induces differentiation, it is necessary to postulate that a system for recognizing tolerated antigens resides in the undifferentiated cell. Furthermore, the recognition system must be complete in every cell for every autogenous substance and must have at least three additional properties: (i) a specificity equal to that of antibodies, (ii) an inability to be overloaded or competitively inhibited by an excess of "self," and (iii) a flexibility sufficient to add and subtract elements for the recognition of foreign substances depending on the latter's presence or absence in the cell's environment.

The alternative to antigen-induced differentiation is a progressive differentiation which is either spontaneous or induced by inherited mechanisms similar to those which cause other forms of differentiation in multicellular organisms. This inherently requires that antibodies be considered naturally occurring proteins. The advantage of this hypothesis is that it permits the control of dif-

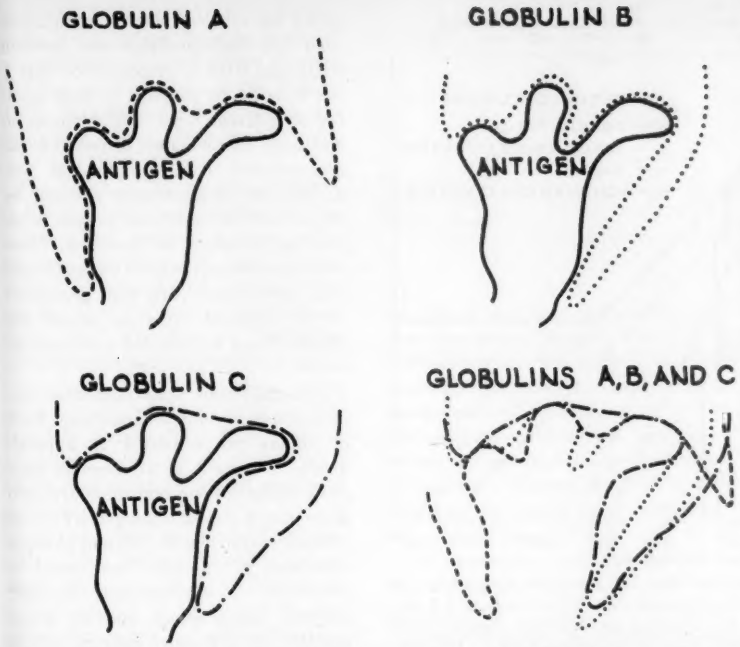

Fig. 1. Two-dimensional diagram illustrating the concept that the information and net specificity possessed by a combination of three different globulin molecules is greater than that possessed by one.

ferentiation, which must be present in any case, to substitute for the complex recognition system required by the first hypothesis. For if the combination of antigen with the first antibody formed in the early stages of differentiation has the effect of inhibiting this differentiation, the specificity and other characteristics of immune tolerance can be explained without postulating a second recognition system. As suggested by Burnet (*19*) and by Lederberg (*20*), the inhibition of partially differentiated cells might be considered a specialized example of hypersensitivity which results in selective destruction of these cells. The same result would be obtained if the "hypersensitivity" was a stimulus to another channel of differentiation. An analogy to the latter phenomenon is the inhibition of antigen development in paramecia grown in the presence of specific antisera (*21*). The action of antigen in suppressing differentiation would explain the requirement of its continued presence to maintain acquired immune tolerance. The persistence of antigen would be required if differentiation of antibody-producing cells was initiated approximately at birth and was continued throughout the life of the animal.

The concept of autogenously controlled differentiation of antibody-producing cells provides a highly satisfactory explanation for the large increase in mitoses observed in lymphatic tissue following an antigenic stimulus. If cell differentiation occurs without antigen, each individual cell type will account initially for a small fraction of the total cell population. Only by a replication of selected differentiated cell types can the capacity to produce the corresponding antibody be increased. Replication without prior differentiation is not adaptive. Replication of a cell differentiated by antigen is an unnecessary adaptive effort. The only alternative to replication of predifferentiated cells would seem to be the concept that replication is a necessary part of antigen induced differentiation.

One of the most important problems in experimental immunology today is the design of experiments to distinguish between the alternatives described above —that is, to determine the role of antigen in cell differentiation. An extension of the work of Nossal and Lederberg to two or more antigenic determinants on the same antigen or to two different antibody molecules to the same determinant would yield important information. An alternative approach is the study of immune tolerance to cross-reacting antigens and of the selective inhibition of only a fraction of the many different antibodies made to the same antigen. From the latter experiments it might be possible to determine whether acquired tolerance is the placing of a particular determinant within a self-recognition system or the selective suppression of pre-existing molecular types of natural globulin.

The major difference between the two hypotheses is that in the first instance antibody production is considered a unique biological phenomenon for which unique mechanisms may be postulated, and in the second it is considered a highly specialized example of certain general cellular processes. The ability of antibodies to distinguish an almost unlimited number of different antigens has always seemed ample justification for the first view. However, the intrinsic unlikelihood of a truly unique biological process and the difficulties presented in even defining an antibody are justification for an attempt to develop the alternative. Because an understanding of the alternative hypothesis requires an alternative concept of immunological specificity, the remaining portion of this article is an attempt to explain immunological specificity on the basis of a limited number of different naturally occurring globulin molecules.

Unique Combinations of Master Molecules

As a basis for immunological specificity the alternative to a unique antibody for each distinguishable antigen is a combination of naturally occurring globulin molecules which is unique for each antigen. The latter concept is based on the following premises.

1) A relative stable complex between a globulin molecule and some other substance can occur whenever the configurations of the two molecules permit the development of short-range intermolecular forces in excess of some critical amount. These forces have been discussed in detail by Pauling (*22*) and by Pressman (*23*).

2) The formation of a stable complex does not require a perfect fit between two complementary configurations (*23*). The heterogeneity of the antibodies combining with a single haptene and the reactions of the same antibody with differ-

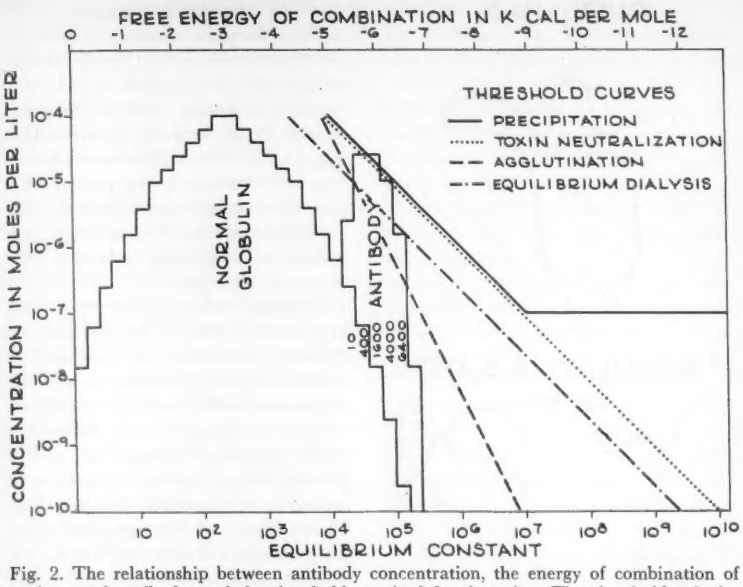

Fig. 2. The relationship between antibody concentration, the energy of combination of antigen and antibody, and the threshold required for detection. The threshold calculations are based on the Goldberg theory and the following assumptions: Agglutination involves a suspension of 10^8 particles per milliliter, each particle containing 6×10^5 sites; precipitation and toxin neutralization involve antigen molecules with a valence of 6 and antibody molecules with a valence of 2, and an optimal ratio of antigen to antibody; equilibrium dialysis requires the binding of at least 20 percent of the haptene in the antiserum compartment.

ent haptenes (*1*) provide experimental evidence for this premise.

3) A single globulin molecule may combine with a large number of different substances in the same sense that a master key may open a large number of different locks. There should be many different antigenic configurations structurally suited to combine with the same globulin if a lack of perfection in the fit in one area may be compensated by an increased binding energy elsewhere.

4) In a mixture of a large number of different globulin molecules, the dominant reactivity will be that common to the largest number of the molecules present. This is because the reactions between antigens and antisera are strongly dependent on concentration and have as well sharp thresholds below which no reaction can be detected.

5) The specificity of an antiserum containing a mixture of different globulin molecules is likely to be very much greater than that of an antiserum in which all the molecules are exactly alike. (See Fig. 1.) This follows from the probability that the number of reactivities common to all of the different molecules will be greatly restricted compared with the number of reactivities possessed by a single molecule.

6) The number of different dominant reactivities and hence the number of antigens which may be distinguished by a system of different globulin molecules is the number of different combinations in which these molecules can be mixed.

On the basis of the premises listed above, the requirements for producing an almost unlimited variety of immune sera are a moderately large number of different natural globulins with overlapping reactivities and a mechanism for selectively increasing the production of those globulins with high affinity for the antigen injected. The total number of different globulin molecules required is determined by three factors: (i) the number a of combinations required to account for the almost unlimited distinguishing ability of immune sera; (ii) the fraction b of all possible antigenic configurations with which the average globulin molecule can combine, which should be approximately equal to the fraction of different globulin molecules with which the average antigen can combine; and (iii) the number c of different globulin molecules in the average monospecific antiserum. Unfortunately, very little is known about these factors except that a is very large. It is implicit in this formulation that b is much larger than $1/a$ and probably lies between 0.001 and 0.01; it is postulated that c lies between 10 and 100. A large number of different types of globulin in an antiserum has the effect of reducing the concentration of each individual type so that the concentration reacting by chance with an unrelated antigen is below the threshold of detection. However, a structurally related antigen might react with a sufficiently high percentage of the different types to exceed the threshold and be detected in a cross-reaction.

If each globulin is so constructed that its reactions at some arbitrarily low level of affinity are restricted to approximately 1 percent of all possible antigenic configurations, and there are 5000 molecular types, each antigen will react with approximately 50 different globulin molecules. In this case there would be $5000^{50}/50!$ or approximately 3×10^{120} different combinations and an equal number of different antigens which could be distinguished. Since this is larger than the number of electrons the universe is thought to contain, it is a satisfactorily large number. If the fraction of antigens which can combine with a single type of globulin molecule is less than 0.01, somewhat more than 5000 different natural globulins are required.

In Fig. 2, the process of immunization is pictured as accelerating the production of a selected fraction of normal globulins until the concentration of these globulins exceeds the threshold required for detection. Threshold curves for precipitation and agglutination can be calculated from the Goldberg theory (*24*) if certain assumptions are made concerning the valence of the antigen and the ratio of antigen to antibody used in the test procedure (*4*). The mean equilibrium constant for antibody is that obtained experimentally by Nisonoff and Pressman for *p*-iodobenzoate (*25*). The exact shape of the distribution curve for normal globulins is unknown and undoubtedly varies according to the antigen used and the genetic and environmental history of the individual. With many antigens the distribution curve for normal globulin crosses the threshold required for agglutination but only rarely the threshold required for precipitation. The selective increase in rate of production during the process of immunization represented in Fig. 2 is analogous to the induction of enzyme synthesis in bacteria. The factor by which the rate of

production is increased by the inductive action of the antigen might be expected to be proportional to the energy of binding. The small numbers in the middle of Fig. 2 represent the factor of increase required to convert the normal globulin curve into the antibody curve.

The possession by protein molecules of affinities for a large number of substances is well recognized. Serum albumin has been shown to bind a large number of natural and synthetic substances (*26*). The number of substances which bind effectively to individual globulin molecules appears to be much more restricted, due perhaps to a greater rigidity of the molecule, as suggested by Karush (*27*). This results in a greater specificity of that binding which does occur. A similar degree of specificity was found by Boyd (*28*) in a study of a large number of plant proteins. Some possessed a highly specific agglutinating ability for red cells containing antigens A, A_1, H, and N. Boyd called these plant proteins lectins from the Latin word *legere*, "to select," and suggested that the name might be used to include "those normal antibodies of animal serum thought not to result from antigenic stimulus." In the case of serum globulins, the restricted number of substances an individual globulin will bind is compensated for by the much greater heterogeneity of the globulins. Thus, it is not surprising that normal serum contains in its globulin fraction agglutinins for the red blood cells of other species and for many bacteria. When the specificity of these agglutinins was demonstrated by his absorption experiments, as depicted in Table 1, Malkoff (*29*) reached the conclusion that a normal serum contains as many specific agglutinins as there are sorts of cells that are agglutinated by the serum. Because of the large number of different substances which could be specifically agglutinated, and because each of them amounted to several micrograms per milliliter of serum, Landsteiner rejected this hypothesis. He was able to purify the agglutinins by absorption and elution from red cells and to show that the purified agglutinins acted most strongly on the red cells used for absorption, but also agglutinated other sorts of blood. He concluded that "if one assumes that normal serum contains a sufficient number of agglutinins, each reacting with a certain proportion of all bloods, a given sort of blood will absorb from a serum all those agglutinins for which it has affinity and there will remain after absorption some that react with freshly added blood of other species. . . . One may conjecture that there exists a much greater variety of globulin molecules in a serum than would appear from physicochemical examination, some of which by virtue of accidental affinity to certain substrates are picked out as antibodies" (*1*, pp. 129, 133).

Table 1. Malkoff's results (*29*).

Blood	Unabsorbed serum	Goat serum absorbed with: Pigeon blood	Rabbit blood	Human blood	Pigeon and rabbit blood	Pigeon and human blood
Pigeon blood	+	0	+	+	0	0
Rabbit blood	+	+	0	+	0	+
Human blood	+	+	+	0	+	0

The preceding conclusion of Landsteiner attributed the specificity of natural antibodies to unique combinations of natural globulins. An extension of this concept to include immune antibodies might have seemed likely, because of the similarity of Landsteiner's own results with synthetic haptenes to those of Malkoff with natural agglutinins (see Tables 1 and 2). However, Landsteiner rejected this concept as an explanation of the specificity of immune antibodies, apparently because of a firm conviction that immune antibodies were different from natural antibodies. More recently, because of the failure to find differences between immune and natural antibodies, all natural antibodies have been considered to be immune antibodies produced in response to the antigens of food or intestinal bacteria. The other alternative, that all immune antibodies are unmodified natural globulins, is the thesis of this article.

Landsteiner was one of the first to demonstrate the heterogeneity of antibodies produced in response to a single antigenic determinant. A classical experiment is reproduced in Table 2 (*30*). This experiment demonstrated that antibodies to a single determinant were heterogeneous with respect to their ability to cross-react with related chemical groupings. Heterogeneity in another dimension—that is, with respect to combining constants—has been amply demonstrated by the more quantitative techniques of precipitation inhibition and equilibrium dialysis. More recently, Nisonoff and Pressman (*31*) have been able to confirm with equilibrium dialysis the experiments of Landsteiner and van der Scheer. Using a radioactively labeled *p*-iodobenzoate, Nisonoff and Pressman showed that an antiserum to this determinant was heterogeneous with respect to the ratio of combining constants to two related substances.

In general, a determination of the combining constants between purified antibodies and various haptenes has shown that the haptene used in the

Table 2. Results obtained by Landsteiner and van der Scheer (*30*). Since the test antigens contained the same proteins, unrelated to the horse serum used for immunization, the protein component could not be responsible for the differential reactions.

Immune sera for *m*-aminobenzene sulfonic acid after absorption with	Azoproteins made from chicken serum and: *o*-Aminobenzene sulfonic acid	*m*-Aminobenzene sulfonic acid	*m*-Aminobenzene arsenic acid	*m*-Aminobenzoic acid
o-Aminobenzene sulfonic acid*	0	++±	±	+
o-Aminobenzene sulfonic acid†	0	+++±	±	+
m-Aminobenzene arsenic acid*	+±	+++	0	+
m-Aminobenzene arsenic acid†	++	++++	0	+±
m-Aminobenzoic acid*	+±	+++	±	0
m-Aminobenzoic acid†	++	++++	±	±
Unabsorbed immune serum*	++	+++±	+	+±
Unabsorbed immune serum†	+++	++++	++	++±

* After standing 1 hour at room temperature.
† After standing overnight in the icebox.

azoprotein antigen for immunization and purification had a higher affinity for the purified antibodies than for any other haptene (*32*). Any modification of the original haptene usually resulted in a lower affinity for the antibodies in proportion to the degree of modification. Occasionally, however, a modified haptene was found with a higher affinity for the antibodies than the haptene used for immunization and purification (*33*). Explanations based on the concept of antibodies as uniquely modified globulins have been possible in most instances but not always (*23*). However, these results are necessary and predictable from the concept of antibodies as natural globulins. It would be expected that those globulins which have been selected by immunization and purification would have the highest average affinity for the haptene used for selection. Since this affinity is due to chance, however, it would also be expected that some of the selected globulins would have a greater affinity for some other haptene. A less likely event, but one which should occur occasionally, is that the majority of selected globulins would have a higher affinity for a haptene other than that used for selection.

If antibodies to synthetic haptenes are natural globulins selected because of a chance affinity for the antigen, it would be expected that unselected globulin (that is, globulin from an untreated animal) would have definite although lower average affinity for these substances. However, the binding of synthetic haptenes to gamma globulin may be impossible to demonstrate unambiguously because the degree of binding falls off rapidly below a critical threshold concentration. As is illustrated in Fig. 2, it might be impossible to detect the reaction between haptene and gamma globulin even though the average energy of combination were one-half that between haptene and purified antibody.

Since the total concentration of gamma globulin usually approximates 10^{-4} moles per liter, the concentration of each individual type of globulin in "normal" serum would be more than 10^{-8} moles per liter if we assumed that there were 5000 different types equally represented. However, the distribution in normal serum is undoubtedly uneven between the various types because of the uneven effect of the many internal and environmental stimuli. For example, the most avid form of diphtheria antitoxin can be detected at a concentration of 10^{-10} moles per liter (*34*). In order to explain its absence in normal serum, it is necessary to postulate that the so-called normal globulins include only those induced by fortuitous exposure to common environmental antigens in food and bacteria. In this respect a toxic substance is a selected antigen. It would not be toxic if it were antigenically similar to the common environmental antigens.

It is tempting to speculate on the relationship between specificity, heterogeneity, inducibility and acquired tolerance. At one end of the spectrum albumin has a concentration which is fixed by some internal homeostatic mechanism. It is therefore not inducible by environmental substances. It has low specificity and low heterogeneity and it is molded to self-tolerance by heredity. At the other end of the spectrum are the gamma globulins. Because of a high specificity, a large number of different types of molecules are required. Because of this heterogeneity, the economy of the animal prevents every one from being present in a high concentration. It is, therefore, advantageous that they be highly inducible. An acquired process such as immune tolerance may be the most efficient mechanism of eliminating harmful types of inducible proteins. Do the globulins in the alpha and beta fractions possess intermediate degrees of specificity, heterogeneity, and inducibility? Properdin may be a case in point. It would be of interest to determine whether the production of such a protein could be inhibited by the mechanisms of immune tolerance.

Summary

The concept of immunological specificity based on a unique combination of natural globulins is an attractive alternative to the classical concept of unique globulin molecules for each possible antigen. Many hitherto separate facets of the antibody response such as antibody diversity, cross-reactions, natural antibodies, increased mitoses in lymphatic tissue, the anamnestic response, and immune tolerance may be related through the general thesis that antibody production is not a unique biological phenomenon but a highly specialized example of certain general cellular processes.

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35. This work was done with the support of grant E-1378 from the National Institute of Allergy and Infectious Diseases, National Institutes of Health.

Genes and Antibodies

Do antigens bear instructions for antibody specificity or do they select cell lines that arise by mutation?

Joshua Lederberg

An antibody is a specific globulin which appears in the serum of an animal after the introduction of a foreign substance, an antigen (*1*). Each of the many globulins is specified by its reaction with a particular antigen (*2*). Our present concern is to formulate a plausible mechanism for the role of the antigen in evoking large amounts of a specific complementary globulin. An important element of any theory of antibody formation is its interpretation of self-recognition, the means by which an organism discriminates its own constituents from the foreign substances which are valid stimuli of the immune response.

Recent speculation about antibody formation (*3–8*) has been dominated by instructive theories which suppose that the antigen conveys the instructions for the specificity of the globulin synthesized under its governance. Elective theories date from Ehrlich (*9*) and have been revived principally by Jerne (*10*), Talmage (*2, 11*), and Burnet (*12*). These postulate that the information required to synthesize a given antibody is already inherent in the organism before the antigenic stimulus is received, and the stimulus then functions to stimulate that mechanism electively. Jerne had proposed an elective transport of antibody-forming templates to functioning sites; Talmage and Burnet have explicitly proposed an elective function based on cellular selection. The details which distinguish the various proposals are pointed out in the following discussion.

Immunology does not suffer from a lack of experimental data, but still some of the most elementary questions are undecided, and it is not yet possible to choose between instructive and elective theories. However, the latter have had so little expression in the past few decades that a detailed exposition may serve a useful function, if only as a target for experimental attack. This article is an attempt to formulate an elective theory on the basis of genetic doctrines developed in studies of microbial populations.

Of the nine propositions given here, only number 5 is central to the elective theory. The first four are special postulates chosen as an extreme but self-consistent set; however, they might well be subject to denial or modification without impairing the validity of the elective approach. The last four propositions are stated to account for the general features of antibody formation in cellular terms and may be equally applicable to instructive and elective theories. If this theory can be defended, and I know of no fatal refutation of it, then clearly elective theories of antibody formation perhaps less doctrinaire in detail should have a place in further experimental design, each proposition being evaluated on its own merits. I am particularly indebted to Burnet (*13*) for this formulation, but Burnet should not be held responsible for some elaborations on his original proposal, especially in propositions 1 through 4. A connected statement of the nine propositions is given in Table 1, and each one is discussed in detail in the following sections.

Antibody Globulin

A1. *The stereospecific segment of each antibody globulin is determined by a unique sequence of amino acids.*

This assertion contradicts the more popular notion, and the usual basis of instructive hypotheses, of a uniform sequence subject to differential folding. The chemical evidence is far from decisive. For example, Karush (*14*) rejects this proposition not on analytical evidence but on the cogent argument that miscellaneous antigenic compounds can scarcely convey instructions for sequence. But if instructive-sequence is implausible, this perhaps argues against instruction rather than differential sequence. Karush has also demonstrated the remarkable stability of antibody through cycles of exposure to denaturing concentrations of urea. He attributes the structural continuity to stabilizing disulfide linkages, but determinant amino acid sequences may also be involved.

Elective antibody formation is of course equally compatible with sequence or folding. In such a theory, the mechanism of assembly does not have to be specified, so long as the product (the prospective antibody) recognizes—that is, reacts with—the antigen. Differential sequence is proposed (i) to stress the ambiguity of present evidence and (ii) as being more closely analogous to current conceptions of genically controlled specificity of other proteins (*15*).

The direct analysis of antibody structure by physicochemical methods has been equivocal. The fractionation of globulins by partition chromatography (*16*) might be interpreted by differential exposure of phenolic, amino, and carboxyl groups rather than differences in essential composition. Characterization of amino acid composition has given sharply different results with rabbit globulins, on the one hand, and equine and human globulins, on the other. Rabbit globulins, including various antibodies, apparently have a uniform N-terminal sequence, so far identified for five residues as (*17*):

Alanine-leucine-valine-aspartic-glutamyl

Various antibodies were, furthermore, indistinguishable in over-all composition (*18*). Any chemical differences would then have to attach to a central, differential segment. This possibility is made more tangible by Porter's recent finding (*19*) that rabbit antibody globulin could be split by crystalline papain into three fragments. One of these was crystallizable (and presumably homogeneous), devoid of *antibody* activity, but equivalent as an *antigen* to the intact globulin. The remaining fractions were more heterogeneous and retained the antigen-combining specificity of the intact antibody. As these fractions may well correspond to the differential segments, their

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Table 1. Nine propositions.

A1. The stereospecific segment of each antibody globulin is determined by a unique sequence of amino acids.

A2. The cell making a given antibody has a correspondingly unique sequence of nucleotides in a segment of its chromosomal DNA: its "gene for globulin synthesis."

A3. The genic diversity of the precursors of antibody-forming cells arises from a high rate of spontaneous mutation during their lifelong proliferation.

A4. This hypermutability consists of the random assembly of the DNA of the globulin gene during certain stages of cellular proliferation.

A5. Each cell, as it begins to mature, spontaneously produces small amounts of the antibody corresponding to its own genotype.

A6. The immature antibody-forming cell is hypersensitive to an antigen-antibody combination: it will be suppressed if it encounters the homologous antigen at this time.

A7. The mature antibody-forming cell is reactive to an antigen-antibody combination: it will be stimulated if it first encounters the homologous antigen at this time. The stimulation comprises the acceleration of protein synthesis and the cytological maturation which mark a "plasma cell."

A8. Mature cells proliferate extensively under antigenic stimulation but are genetically stable and therefore generate large clones genotypically preadapted to produce the homologous antibody.

A9. These clones tend to persist after the disappearance of the antigen, retaining their capacity to react promptly to its later reintroduction.

further immunological and chemical analysis will be of extraordinary interest.

In contrast to the uniformity of rabbit globulins, normal and antibody globulins of horse serum proved to be grossly heterogeneous but equally so, a wide variety of N-terminal groups being found in all preparations (*20*). This merely confirms the concept of the plurality of antibodies evoked by a given antigen, which have in common only the general properties of normal gamma globulins and the capacity of reacting with the evoking antigen. The globulins of man, and in particular the characteristic globulins produced by different patients suffering from multiple myeloma, are likewise recognizably different, inter se, in amino acid composition (*21*).

Gene for Globulin Synthesis

A2. *The cell making a given antibody has a correspondingly unique sequence of nucleotides in a segment of its chromosomal DNA: its "gene for globulin synthesis."*

This postulate follows plausibly from proposition A1, and would trace antibody-forming specificity to the same source as is imputed to other specific proteins. As the most deterministic of genetic hypotheses, it should be the most vulnerable to experimental test. For example, a single diploid cell should be capable of *at most* two potentialities for antibody formation, one for each chromosome.

In tests of single antibody-forming cells from rats *simultaneously* immunized against two *Salmonella* serotypes, Nossal and I (*22*) could find only monospecific cells producing one or the other antiflagellin. Coons (*23*) and White (*24*) have reached a similar conclusion in applications of fluorescent labeling technique. However, Cohn and Lennox (*25*) have convincing evidence for some bispecific antibody-forming cells in rabbits *serially* immunized against two bacteriophages. Experiments pertinent to the possibility of a single cell's carrying more than two antibody-forming specificities remain to be done (*26*).

The chromosomal localization of antibody-forming specificity is uncoupled from its elective origin in proposals (*7, 8, 27*) that an antigen induces a mutation in a gene for globulin synthesis, though not necessarily involving a new nucleotide sequence.

Multiple specificity would stand against a simple chromosomal basis for antibody formation (*28*), leaving two alternative possibilities: (i) replicate chromosomal genes or (ii) extrachromosomal particles such as microsomes. These might best be disentangled by some technique of genetic recombination.

The differentiation of microsomes must be implicit in any current statement of a theory of antibody formation that recognizes their central role of protein synthesis. The main issue is whether or not their specificity is dependent on that of the chromosomal DNA. Autonomy of microsomes, in contradiction to proposition A2, is implicit in most instructive theories, the microsome carrying either the original or a copy of the antigenic message. On the other hand, a powerful elective theory is generated by substituting the term *microsomal RNA* for the terms *chromosomal DNA* and *gene* in the various propositions. Since a single cell may have millions of microsomes, this theory would allow for any imaginable multiplicity of antibody-forming information in a single cell. If the potential variety of this information approaches that of the total antibody response, further instructions in an antigenic input would become moot. In addition, the complexities of selection of cellular populations would be compounded by those of microsomal populations within each cell. These degrees of freedom which blur the distinction between microsomal instruction and election favor the utility of the chromosomal hypothesis as a more accessible target for experimental attack.

Genic Diversity of Precursor Cells

A3. *The genic diversity of the precursors of antibody-forming cells arises from a high rate of spontaneous mutation during their lifelong proliferation.*

Three elements of this statement should be emphasized: (i) that antibody-forming cells are specialized, (ii) that their diversity arises from some random process, and (iii) that the diversification of these cells continues, in company with their proliferation, throughout the life of the animal.

Item (i) and its justification by various experiments have already been discussed as an aspect of proposition A2. Talmage (*2*) also stresses the specialization of antibody-forming cells by referring to their progressive *differentiation*. This is entirely consistent with propositions A3 and A4, which then postulate a specific mechanism of cellular differentiation, in this case, gene mutation. If, on Talmage's model, fully differentiated cells are ultimately left with no more than one antibody-forming specificity per chromosome, the general consequences will be the same whether this final state represents the unique activation of one among innumerable chromosomal loci (see *27*) or the evolution of one among innumerable specific alleles at a given locus. Once again, the final resort for decision may have to be a recombinational technique.

If the discrepancy between the experiments of Nossal and Lederberg (*22*) and those of Cohn and Lennox (*25*), as dis-

cussed under proposition A2, is real and depends on the timing of immunization, it may furnish strong support for (ii), the random origin of antibody-forming specificity. If antibody-forming cells can have two (or any small number of) specificities randomly derived, only a negligible proportion will have just the two being tested for. This would correspond to the case of simultaneous immunization with the two test antigens. If, however, a population of cells carrying one specificity is selected for, followed by selection for a second specificity among all available cells, this is the case of serial immunization and is precisely the method one would predict to obtain a clone "heterozygous" for two mutant alleles. Simultaneous versus serial immunization would be analogous to the suppression versus selection of bacterial mutants resistant to two antibiotics (*29*). Further experiments are needed to exclude more trivial reasons for the scarcity of bispecific antiflagellin-forming cells.

Item (iii) diverges from Burnet's proposal that the "randomization" of antibody-forming cells is confined to *perinatal* life, thereby generating a set of then stable clones corresponding to the antibody-forming potentiality of the animal. These clones would then be irreplaceable if lost either by random drift or as a consequence of premature exposure to the corresponding antigen. The arguments against Burnet's proposal are by no means decisive; however, the correspondence between cells and antibodies is made more difficult by having to maintain each clone at a sufficient population size to compensate for loss by random drift. Further, the recurrence of antibody-forming specificity is supported by experiments showing the decay of immune tolerance in the absence of the corresponding antigen (*30*; see comment on proposition A6). Since immune reactivity in these experiments may return during adult life, susceptibility to the induction and maintenance of tolerance by the timely introduction of the antigen may have only a coincidental relationship to the immunological incompetence of the newborn animal.

Hypermutability

A4. *This hypermutability consists of the random assembly of the DNA of the "globulin gene" during certain stages of cellular proliferation.*

This *ad hoc* proposal is doubtless the least defensible of the propositions, and certainly the furthest removed from experimental observation. It is stated to illustrate that accurate replication rather than mutability is the more remarkable phenomenon, whatever the detailed mechanism for the variation. If, as has been suggested, many nucleotide triplets are *non*sensical (*31*), the triplets rather than single nucleotides would have to be posed as the unit of assembly in this case.

To carry this speculation one step further, *heterochromatin* has been proposed to be, on the one hand, a random sequence, and, on the other hand, a dissynchronously assembled segment of the genome (*32*). If both views are correct, proposition A4 might be restated: "the globulin gene is heterochromatic during certain stages of cellular proliferation" (becoming by implication, euchromatic in the mature stages of propositions A8 and A9).

For the theory of microsomal election it might be postulated that globulinogenic microsomes are initially fabricated as faulty replicas of the globulin gene, but are then capable of exact, autonomous replication.

Pending more exact knowledge and agreement of opinion on the morphogenetic relationships of antibody-forming cells, the term *certain stages* cannot be improved upon. On the other hand, as is shown under proposition A8, a model might be constructed even on the basis of a constant but high mutation rate of all antibody-forming cells.

Further insight into the mechanism of cellular diversity in antibody formation may be won by studies on the genetic control of reactivity to various antigens in inbred animals (*33*); two cautions, however, must be stated: (i) for effects on the transport of particles of different size, and (ii) for effects from cross-reactions with gene-controlled constituents evoking autotolerance.

Spontaneous Production of Antibody

A5. *Each cell, as it begins to mature, spontaneously produces small amounts of the antibody corresponding to its own genotype.*

Note the implication that antibody is formed prior to the introduction of the antigen into the antibody-forming cell.

The function of spontaneous antibody is to mark those cells preadapted to react with a given antigen, either to suppress these cells for the induction of immune tolerance (proposition A6) or to excite them to massive antibody formation (proposition A7). Therefore, the antigen need participate in no type of specific reaction with cell constituents other than antibody itself, the one type of reaction available to chemically diverse antigens that requires no further special pleading. There is no agreement whether the reactive globulins found in the serum of untreated animals are produced spontaneously or by casual exposure to cross-reacting antigens (see *2*). Accordingly, the spontaneous antibody postulated in proposition A5 may or may not be produced in the quantity and form needed for it to be liberated and detected in the serum. The nonspecific fragment of antibody-globulin described by Porter raises the possibility that the same *determinant* segment may be coupled either to a diffusible or to a cell-bound residue, the latter corresponding to various aspects of cellular immunity, including the suppression or excitation of antibody-forming cells by reactions with the corresponding antigen.

Induction of Immune Tolerance

A6. *The immature antibody-forming cell is hypersensitive to an antigen-antibody combination: it will be suppressed if it encounters the homologous antigen at this time.*

This is the first of four propositions which bear less on the source of antibody-forming specificity than on its subsequent expression in terms of cellular behavior. These propositions are therefore equally applicable to instructive theories.

The duality of reactions of antigens with antibody-forming cells is simply a restatement of the experimental observations of tolerance versus immunity (*34*). It seems plain that every cell of the antibody-forming system must be marked to inhibit its reactivity both to the autologous antigens of the same animal and extraneous antigens introduced and maintained from a suitably early time of development. In the light of current evidence for the persistence of antigenic molecules (*5, 6*) and for the loss of tolerance when a given antigen has dissipated (*30*) there are no more plausible candidates for the self-markers then the antigens themselves. The distinction between the function of an antigen as inhibitor (self-marker) or as inducer of antibody formation is then the time when the antigen is introduced into the potential antibody forming cell. We may profitably define maturity in terms of

the progression of the cell from sensitivity towards reactivity.

The suppression of this process of maturation is a sufficient attribute to account for tolerance, and this need not involve so drastic an event as the destruction of the cell. However, the elective hypothesis proposes that only a limited number of cells will spontaneously react with a given antigen, so that their destruction by premature reaction can safely be invoked as the means of their suppression. It may be hoped that presently documented phenomena of cellular hypersensitivity may furnish a precedent for cellular destruction by such reactions. The cytotoxicity of the antigen to hypersensitive cells is still controversial even in the historical case of tuberculin sensitivity (*35*). However, the destruction of invading *lymphocytes* of the host in the course of rejection of a sensitizing homograft (*36*) supports the speculation of some role of cellular destruction of immature antibody-forming cells in the induction of tolerance.

The nature of immaturity remains open to question. It might reflect the morphogenetic status of the antibody-forming cell—for example, sensitive lymphocyte → reactive plasma cell (*37*), some particular composition of immature sensitizing antibody, or merely a very low level of antibody so that complexes are formed in which antigen is in excess.

Finally, one additional hint of an implication of hypersensitivity in the early stages of the antibody response: the transient skin sensitivity of delayed type (and transferable by cells) appearing in the course of immunization, as observed by several workers (*38*). If these skin reactions reflect the destruction of some antibody-forming cells, it would speak for some overlapping or reversibility of the two stages of maturation.

The implications of proposition A6 in the elective theory may be summarized as follows: If an antigen is introduced prior to the maturation of any antibody-forming cell, the hypersensitivity of such cells, while still immature, to an antigen-antibody reaction will eliminate specific cell types as they arise by mutation, thereby inducing apparent tolerance to that antigen. After the dissipation of the antigen, reactivity should return as soon as one new mutant cell has arisen and matured. As a further hopeful prediction, it should be possible to induce tolerance in clones of antibody-forming cells from adult animals by exposing a sufficiently small number of initials to a given antigen.

Excitation of Massive Antibody Formation

A7. *The mature antibody-forming cell is reactive to an antigen-antibody combination: it will be stimulated if it first encounters the homologous antigen at this time. The stimulation comprises an acceleration of protein synthesis and the cytological maturation which mark a "plasma cell."*

These principles of the cellular response to *secondary* antigenic stimulation are widely accepted and are readily transposed to the *primary* response on the elective hypothesis whereby some cells have spontaneously initiated antibody formation according to proposition A5.

Proliferation of Mature Cells

A8. *Mature cells proliferate extensively under antigenic stimulation but are genetically stable and therefore generate large clones genotypically preadapted to produce the homologous antibody.*

This proposition takes explicit account of the secondary response, the magnitude of which is a measure of the increase in number of reactive cells (*26*). However, the antigen *need* play no direct part in the stabilization of antibody-forming genotype which might accompany the determinate maturation of the cell whether or not it is stimulated. In fact, it may be possible to dispense with the postulate that mature cells are less mutable by adopting a mutation rate which is an effective compromise: to furnish a variety of genotypes for the primary response while selected genotypes may still expand for the secondary response. For example, by mutation of one daughter chromosome per ten cell divisions, on the average, after ten generations about 600 chromosomes of the same type would have been produced, together with 100 new genotypes distributed among the other 400 or so cells. Selection must then compensate for the mutational drift if a given clone is to be maintained.

Persistence of Clones

A9. *These clones tend to persist after the disappearance of the antigen, retaining their capacity to react promptly to its later reintroduction.*

This is a restatement of the possibly controversial phenomenon of lifelong immunity to viruses (*4, 5*). A substantial reservoir of immunological memory should be inherent from one cycle of expansion of a given clone. Its ultimate decay might be mitigated either by continued selection (that is, persistence of the antigen) stabilization of genotypes, or dormancy (to cell division or remutation, or both) on the part of a fraction of the clone.

Discussion

Each element of the theory just presented has some precedent in biological fact, but this is testimony of plausibility, not reality. As has already been pointed out, the most questionable proposition is A4, and it may be needlessly fanciful to forward a too explicit hypothesis of mutability for antibody formation when so little is known of its material basis anywhere.

Theories of antibody formation have, in the past, been deeply influenced by the physiology of inducible enzyme synthesis in bacteria. In particular, instructive theories for the role of the substrate in enzyme induction have encouraged the same speculation about antibody formation. This interpretation of enzyme induction, however, is weakened by the preadaptive occurrence of the enzymes, at a lower level, in uninduced bacteria (*39*).

One of the most attractive features of the elective theory is that it proposes no novel reactions: the only ones invoked here are (i) mutability of DNA; (ii) the role of DNA, presumably through RNA, as a code for amino acid sequence and (iii) the reaction between antibody and antigen, already known to have weighty consequences for cells in its proximity. The conceptual picture of enzyme induction would be equally simplified if the enzyme itself were the substrate-receptor. Clearly, susceptibility to enzymic action is not a necessary condition for a compound to be an inducer —for example, neolactose and thiomethylgalactoside for the β-D-galactosidase of *Escherichia coli* (*39, 40*), but formation of complexes with the enzyme may be. The picture is somewhat complicated by the intervention of specific transport systems for bringing the substrate into the cell (*40*).

Antibody formation is the one form of cellular differentiation which inherently requires the utmost plasticity, a problem for which the hypermutability of a patch of DNA may be a specially evolved solution. Other aspects of differentiation

may be more explicitly canalized under genotypic control. Nucleotide substitution might still play a role here by modifying the level of activity rather than the specificity of neighboring loci, and elective recognition of transient states spontaneously derived then remains as a formal, if farfetched, possibility for other morphogenetic inductions.

References and Notes

1. This definition excludes antibody-like substances such as the hemagglutinins found in normal human sera. These reagents do not, however, pose the problem of the mechanism of specific response which is the burden of this discussion.
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Basic Research in Industry

A count of scientific publications suggests the extent of U.S. industry's effort in basic research.

J. C. Fisher

It is difficult to find out how much basic research is going on in industry in the United States. There are at least three stumbling blocks in the way: different companies do not agree in their definitions of basic research; some companies are not sure how much of it they are doing according to their own definitions; and others are not willing to say even if they know. In spite of these difficulties, the National Science Foundation has made a good statistical study by supplying its own definition, sending out questionnaires, and providing strictly confidential treatment of the replies (*1*). Except perhaps for companies engaged in research in the engineering sciences (such as advanced mechanics, fluid dynamics, and aerothermodynamics), where the National Science Foundation suspects its definition may have been liberally interpreted, the aggregate amounts of basic research in different industries seem to have been established fairly well.

There is more than one name for the body of scientific work that is directed toward increasing our knowledge and understanding of nature. Some call it "learning work." Others call it "scientific research," "basic research," or "fundamental research." The National Science Foundation calls it "basic or fundamental research" and defines it as "projects which are not identified with specific product or process applications, but rather have the primary objective of adding to the overall scientific knowledge of the firm." It found that industry in 1953 employed about 5500 scientists and spent about $150 million for this

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activity, a level of effort amounting to about 4 percent of the nearly $3.7 billion total spent for industrial research and development. Well over half of the basic research was concentrated in the chemical, petroleum, electrical, and aircraft industries, and large companies appeared to be doing most of it. (The National Science Foundation survey did not include scientific and engineering consulting firms or commercial laboratories.)

It would be instructive to know in detail the effort that individual companies devote to basic research. The National Science Foundation study does not reveal this information, because its figures are confidential and are presented in such a way that the contributions of individual companies are hidden. However, there is an independent means for determining the extent of the effort devoted to basic research, based essentially upon the idea that publication of the results of basic research provides a clue to the work that preceded publication. Publications are a matter of record, and it is possible to select and count those that deal with basic research. Insofar as the number of publications originating in a given company is proportional to the quantity of work going on there, this method will work.

Most scientists engaged in basic research have strong motivation for publishing the results of their activities. Through publication they achieve recognition, build their reputations as scientists, and make their work available to others for appraisal. If a scientist's employer does not allow him to publish, he tends to go elsewhere, for without competent appraisal of his work he is at a serious disadvantage and his effectiveness is diminished. For this reason it would seem that a count of publications could give a relatively good picture of the quantity (not quality) and distribution of basic research effort. The analysis now to be described (2) is based upon this assumption, which will be more fully tested and verified as the analysis proceeds.

Method of Counting Publications

Publications were counted indirectly, by counting abstracts (of articles only, not of patents) in the 1955 volume of *Chemical Abstracts*. This journal publishes abstracts of all the world's technical literature that is concerned with "learning" in chemistry, metallurgy, solid-state and nuclear physics, and certain branches of biology and physiology. These fields of science encompass most of the learning carried on by U.S. corporations, save for subjects in the engineering sciences, such as fluid mechanics and aerothermodynamics, and in electron physics. It is only approximately true that *Chemical Abstracts* finds and abstracts all publications concerned with basic research and rejects all publications concerned with applied work. However, the proportion of abstracts dealing with applied work appears to be reasonably small and invariant, so a count of the abstracts should give a fair approximation of the true number of basic research publications.

The procedure followed in counting abstracts was simply to examine the approximately 100,000 abstracts included in the 1955 volume of *Chemical Abstracts* and to prepare a card for each of the approximately 3000 publications whose author was an employee of a company in the United States. (An additional 50 or so articles in electron physics, mostly originating in the Bell Telephone Laboratories, were discovered by examining the appropriate scientific journals.) The engineering sciences are believed to be the only industrially important fields not covered in this survey.

The work represented by the approximately 3000 publications under study probably was performed sometime around 1953, most of the technical articles having been published in 1954,

Table 1. Companies with ten or more basic research publications per year. The approximate numbers of 1954 publications representing basic research in the physical sciences were obtained from *Chemical Abstracts* (1955), the *Bell System Technical Journal*, and five Institute of Radio Engineers publications. These sources do not provide a record of publications that have been classified for security reasons, or that describe the aircraft industry's work in the engineering sciences. Publications from scientific and engineering consulting firms, commercial laboratories, and a few laboratories operated by private companies for the Federal Government (such as General Electric's KAPL and Hanford laboratories and Union Carbide and Carbon's Oak Ridge National Laboratory) have not been counted.

Company (including subsidiaries)	No. of publications	Company (including subsidiaries)	No. of publications	Company (including subsidiaries)	No. of publications
1. General Electric	170	22. Socony Mobil Oil	31	43. Searle (G. D.)	15
2. Bell Telephone Laboratories	134	23. Sterling Drug	31	44. Sun Oil	15
3. DuPont (E. I.) de Nemours	121	24. Ciba Pharmaceutical Products	28	45. Procter and Gamble	14
4. American Cyanamid*	107	25. U.S. Steel	28	46. Sperry Rand	14
5. Merck	90	26. Standard Oil of California	24	47. Blockson Chemical‡	13
6. Eastman Kodak	81	27. Armour	23	48. Esso Research and Engineering§	13
7. Shell Oil	73	28. Olin Mathieson Chemical†	23	49. General Motors	13
8. Monsanto Chemical	65	29. Hercules Powder	22	50. Smith, Kline and French Laboratories	13
9. Union Carbide and Carbon	63	30. Pfizer (Chas.)	22	51. Atlantic Refining	12
10. Dow Chemical	58	31. Schering	22	52. Goodyear Tire and Rubber	12
11. Westinghouse Electric	57	32. General Aniline and Film	21	53. Irwin, Neisler	12
12. Lilly (Eli)	54	33. Humble Oil and Refining	21	54. Allied Chemical and Dye	11
13. Standard Oil (Indiana)	48	34. North American Aviation	21	55. Bristol-Myers	11
14. Rohm and Haas	45	35. Ethyl	20	56. Ford Motor	11
15. Upjohn	44	36. General Mills	19	57. Minnesota Mining and Manufacturing	11
16. Burroughs, Wellcome	35	37. Hoffmann-LaRoche	19	58. Continental Oil	10
17. Radio Corporation of America	35	38. Goodrich (B. F.)	18	59. National Lead	10
18. Sylvania Electric Products	33	39. Gulf Oil	18		
19. Abbott Laboratories	32	40. Aluminum Company of America	17		
20. Parke, Davis	32	41. U.S. Rubber	16		
21. Phillips Petroleum	31	42. American Home Products	15		

* Includes 60 publications from Lederle Laboratories. † Includes 12 publications from Squibb. ‡ Now a division of Olin Mathieson Chemical. § Standard Oil (N.J.) is a holding company and does not itself appear in this list.

the abstracts in 1955. It should be possible, therefore, to make a meaningful comparison with the National Science Foundation study, which also was based upon work done in 1953.

Publications of Individual Companies and Industries

When the publications were grouped by companies, it was found that about 500 companies were represented, most of them by but a single publication. On the other hand, a few companies were very prolific. Table 1 lists all companies represented by ten or more publications, in order of the number provided by each. There are 59 companies in this list, and together they account for just over two-thirds of the total number of publications. Most of them are engaged in pharmaceutical, chemical, petroleum, or electrical enterprise, where the importance of basic research is well recognized.

When the publications are grouped according to industry, the results shown in the first two columns of Table 2 are obtained. The chemical and pharmaceutical industries clearly lead, with, altogether, about 1450 publications, or nearly half the total. The electrical equipment and petroleum industries follow, with about 500 and 400 publications, respectively. All the remaining publications add up to about 700. The third and fourth columns of the table give the cost of basic research in each industry according to the National Science Foundation report, and the cost per publication. Similarly, the last two columns give the number of scientists doing basic research in each industry and the ratio of the number of scientists to the number of publications. Separate figures are given for each of the industries that published significantly more than 100 papers, and all the others are lumped together. The cost-per-publication and scientist-per-publication figures should be fairly reliable, even though the National Science Foundation's classification of firms into industries may differ somewhat from that employed in our study.

The chemical, pharmaceutical, electrical, and petroleum industries produce large numbers of publications, altogether about 80 percent of the total. Their basic research costs run between $26,000 and $38,000 per publication, and each publication represents a year's work for about 1.34 scientists. It is encouraging to find that there is a fixed ratio of basic research scientists (as determined by the National Science Foundation) to basic research publications (as determined by counting abstracts). The existence of this fixed ratio confirms the idea that publications provide a reasonably good measure of the amount of basic research that is going on in these industries, at least statistically on an industry-wide basis. To obtain an estimate of the number of scientists engaged in basic research, all one has to do is to multiply the number of papers published in a year by 1.34.

For the other industries that together produce about 20 percent of the publications, the number of scientists per publication jumps to an average of 3.45 from the average of 1.34 characteristic of the pharmaceutical, chemical, petroleum, and electrical industries. Either

Table 2. Basic research publications, costs, and scientists (by industry).

Industry	No. of publications		Cost		Scientists		
			Total* ($ million)	Per publication (in dollars)	Total†	Per publication	
Chemical	833	1457	37.8	26,000	1990	1.37	1.34
Pharmaceutical‡	624						
Electrical	501		19.1	38,000	660	1.32	
Petroleum	384		11.1	29,000	480	1.25	
Primary metals	117	686§	81.7	120,000	2370	3.45	
Food	108						
Transportation equip.	81						
Fabricated metals	61						
Instruments	61						
Paper	60						
Rubber	57						
Stone, clay, glass	41						
Others and unknown	100						
Total		3028	149.7		5500		

* According to the NSF study. † Derived from (i) basic research costs and (ii) average cost of research and development per scientist or engineer, both as given in the NSF study for the industry in question. ‡ Including Lederle Laboratories and Squibb. § Not including publications relating to basic work in the engineering sciences, of particular importance to the aircraft and instrument industries.

Table 3. Basic research versus company size in four industries. (Quartile No. 1 contains the largest companies in an industry; quartiles No. 2 and 3, the next largest; quartile No. 4, the smallest, down to 1000 employees.)

Quartile No.	No. of companies	No. of employees	No. of publications	No. of scientists per 1000 employees
		*Pharmaceutical industry**		
1	3	34,800	136	5.2
2	3	28,400	41	1.9
3	4	31,100	115	5.0
4	16	30,100	126	5.6
Total	26	124,400	418†	4.5
		*Chemical industry**		
1	3	213,000	260	1.64
2	6	178,000	211	1.59
3	18	197,000	145	0.99
4	82	168,000	102	0.81
Total	109	756,000	718†	1.27
		Petroleum industry		
1	3	173,000	98	0.76
2	6	208,000	159	1.02
3	23	211,000	80	0.51
4	83	188,000	23	0.16
Total	115	780,000	360†	0.62
		Electrical industry		
1	2‡	344,000	304	1.18
2	6	404,000	110	0.36
3	23	371,000	63	0.23
4	155	394,000	11	0.04
Total	186	1,513,000	488†	0.43

* Lederle Laboratories and Squibb are now included with parent companies in the chemical industry. † Slightly less than the total in Table 1 because of the inclusion in Table 1 of companies with less than 1000 employees or of unknown size. ‡ Bell Telephone Laboratories and Western Electric are counted as a single enterprise, comparable to other companies in the electrical industry.

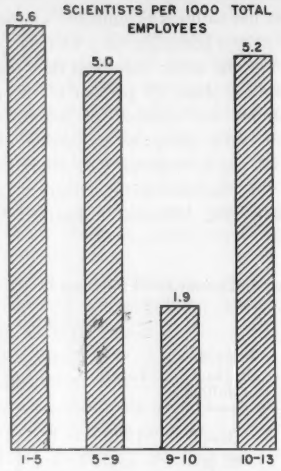

Fig. 1. Pharmaceutical industry quartiles. In most industries, small companies do relatively little learning in proportion to their size. The pharmaceutical industry is an exception. Small and large companies show about the same intensity of effort.

scientists in these other industries publish less, or some of their publications were overlooked (as many of them undoubtedly were, because publications related to basic work in the engineering sciences were not included in the survey), or there was some exaggeration by these industries when they reported their basic research effort to the National Science Foundation. Owing to this uncertainty, further analysis is restricted to the chemical, pharmaceutical, electrical, and petroleum industries. The data are plentiful and reasonably complete for these industries, which employ over 3000 of the 5500 basic research scientists the National Science Foundation finds in all industry. The only industry likely to be seriously slighted by this restriction is the aircraft industry, whose relatively weak showing may result from the poor

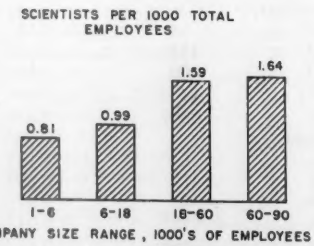

Fig. 2. Chemical industry quartiles. The intensity of effort in learning in small chemical companies is only 50 percent of that of large companies.

coverage of engineering science publications.

If the ratio of scientists to publications were 1.34 for each of the individual companies listed in Table 1, the numbers of basic research scientists employed by each company would range from about 230 for General Electric down to about 13 for National Lead. Confidential information concerning the number of basic research scientists actually at work in the laboratories of some of these companies suggests that the factor 1.34 gives surprisingly good results when applied to individual companies and may perhaps be relied upon to an average accuracy of 20 percent or so.

In the light of the relationship between publications and scientists just established, it is instructive to examine Table 1 again with the object of converting the numbers of publications to (i) numbers of basic research scientists and (ii) dollars per year spent for basic research. The conversion factors are, roughly, 1.34 scientists per annual publication; $26,000 per publication (chemical and pharmaceutical); $38,000 per publication (electrical); and $29,000 per publication (petroleum). In other words, in 1953 the basic research staffs of the companies listed in Table 1 ranged from about 230 to about 13 scientists and the basic research budgets of these companies ranged from about $6.5 million to about $0.3 million.

Role of Company Size

The present analysis bears out the National Science Foundation's observation that most basic research is done in large companies. In order properly to show how the intensity of basic research effort depends upon company size, it was necessary to obtain a reasonably complete list of all the companies in each industry—whether or not they did any basic research—together with the number of employees in each company. Lists of this type were prepared for each industry by examining *Poor's Register of Directors and Executives* (*3*). About 1800 companies of 1000 or more employees were listed and classified. Nonmanufacturing companies and companies with fewer than 1000 employees were not counted. The industry to which each company belonged was determined from the list of products given in *Poor's*. The large companies were checked again in the second *Fortune* directory of the 500 largest U.S. manufacturing companies

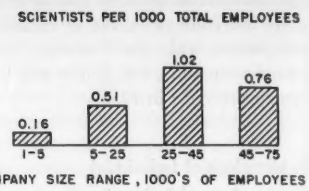

Fig. 3. Petroleum industry quartiles. The intensity of effort in learning in small petroleum companies is only 20 percent of that of large companies.

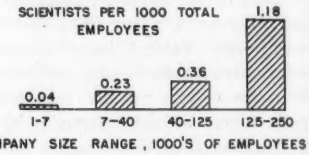

Fig. 4. Electrical manufacturing industry quartiles. The intensity of effort in learning in small electrical manufacturing companies is only 3 percent of that of large companies.

(*4*), and where *Fortune's* figures for the number of employees differed from *Poor's*, *Fortune's* figures were used.

The companies in each industry were divided into quartiles, containing as nearly as possible equal numbers of employees. The first quartile contained the largest companies, the second the next largest companies, the third the next largest, and the fourth the smallest companies, down to 1000 employees. For each quartile the following figures were assembled: number of companies, number of employees, number of publications, and number of basic research scientists per 1000 total employees. The last figure was derived on the assumption that one publication corresponds to 1.34 scientists. All these data are presented in Table 3, and the ratios of scientists to total employees are shown graphically in Figs. 1–4.

The information in Table 3 and in Figs. 1–4 shows that small companies engage in learning activity to a much greater degree in some industries than in others. In the pharmaceutical industry, for example, the average intensity of effort is as great in companies of 1000 employees as it is in the largest companies. This uniform distribution of learning activity was not found in any other industry. In the chemical industry, the small companies do only about half as much learning *per employee* as the large companies; in the petroleum industry they do only about 20 percent as much; and in the electrical manufacturing industry, only about 3 percent as much.

One possible explanation for the small amount of learning done in small companies in some industries is that these companies buy their learning from outside agencies instead of doing it themselves. The National Science Foundation study casts considerable doubt upon the validity of this explanation, however.

Whatever the reason for the small learning effort in small electrical manufacturing companies, it is an economic fact. There appears to be a critical company size, for research effort, of very roughly 20,000 employees; companies with more than 20,000 employees sometimes do learning work at the same rate as large companies, but smaller companies almost never do. Of the 170 companies in the 1000-to-20,000-employee class, only two (Hughes Tool and Sprague Electric) come up to the average of the largest companies in intensity of effort. For petroleum companies the critical size is very roughly 5000 employees; only 4 of 83 companies in the 1000 to 5000 employee come up to the level of the top two groups in intensity of effort. For chemical companies there is no true critical size, but it is roughly at the 4000-employee level that the intensity of effort drops to half that in the top two groups.

Factors Favoring Research Support

So much for the factual presentation of data. What is revealed about the conditions under which industry finds it profitable (or thinks it profitable) to do basic research? It appears that two important requirements must be met. (i) The industry must be one in which innovation and associated obsolescence proceed rapidly. (The pace of innovation and obsolescence is very rapid in the pharmaceutical industry and moderately rapid in the chemical, petroleum, electrical manufacturing, and aircraft industries. These are the industries in which basic research flourishes. The pace in other industries is slow by comparison.) (ii) The company must be sufficiently large and diversified. (For pharmaceutical companies, almost any size seems to be large enough, but for electrical manufacturers, anything less than about 20,000 employees is definitely too small. It seems probable that small electrical manufacturing firms are poorly diversified in their activities and cannot make efficient use of the relatively unpredictable results of basic research.)

These two requirements seem reasonable. A company in a slowly developing industry need do no basic research. Innovations are few and far between, and it is more profitable to copy those adopted in other plants than to try to be first. Even in a fairly rapidly developing industry, it may be wise for small companies to wait until innovations appear, and then to copy them. Only the large competitors of such companies have both the resources for supporting an integrated research program and the wide diversification that enables them to take advantage of the products and by-products of basic research.

Size does not seem to be a factor in the pharmaceutical business. Perhaps this is because the pace in this field is so rapid that there is no time to copy one's competitors; by the time a competitor has been copied the product is obsolete. If a company does no basic research, it falls by the wayside.

Basic research in industry is a relatively new activity, which was almost unknown in 1900. It has grown to the point where in 1953 somewhere near $150 million a year was invested in it, in spite of the fact that a decade or so must elapse between the beginning of a research program and the point at which the possibility of practical results, if any, can first be glimpsed. The work is done by scientists whose motivation lies in science, not in economics. Yet such work is generally believed to be a sound investment for diversified companies in rapidly expanding industries, and it may even be necessary for survival in the pharmaceutical business.

Time alone will show how rapidly industry's rate of investment in basic research will grow, and by how much it will exceed industry's present value of 4 percent of its total expenditures for research and development.

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News of Science

Five Euratom Nations Consider Reactor Construction

Euratom, a six-nation cooperative organization set up to bring atomic power to Europe, has received letters of intention indicating that five of the member nations have "enterprises" within their borders that plan to submit proposals for reactors to be built under the Euratom–U.S. Joint Nuclear Power Program. The five nations are Belgium, France, Germany, Italy, and the Netherlands. Luxembourg did not submit a letter of intention. The term *enterprise*, which was used in an official announcement of the receipt of the letters, was not further defined.

Letters of intention for the proposals were submitted 28 May to Euratom headquarters in Brussels. These letters, however, as AEC authorities here stress, do not constitute commitments to build. They are submitted only to give Euratom officials some indication of response to the program. This was less enthusiastic than U.S. officials had hoped, according to observers. Members of the Atomic Energy Commission had hoped for six to eight proposals, to ensure an active role for the European power agency. The U.S., through an Export-Import loan, is providing $135 million in financial aid for the program.

The question that hung on the letters of intention was this: did European utilities find the offered United States

financial assistance a sufficient inducement to proceed with expensive reactor development on a sizable scale? The answer seems to be a qualified "yes."

Obsolescence Feared

Reports from Europe have indicated that many producers of electric power were reluctant to invest large sums in types of reactors that might be surpassed in efficiency in a short time. This reluctance, along with other factors—for example, the changes in the European power-supply situation since Euratom was conceived, during the oil shortage coincident with the Suez crisis—has threatened to upset the schedule originally devised for European nuclear development. The Euratom pact, an "agreement for cooperation," provides that the proposed reactors should be in operation by 31 December 1963. Under provisions of an exemption, completion of two reactors may be deferred until 1965.

According to this time schedule, if there is follow-through on all five letters of intention, there should be at least three power reactors in operation in Europe by the beginning of 1964. It remains to be seen whether this amount of activity will be sufficient to convince American legislators that financial aid for the Euratom program should be continued and expanded. Recently, the Joint Congressional Committee on Atomic Energy proposed that there be a substantial slowing down of U.S. aid to the research and development aspect of the program, on the grounds that Euratom has fallen behind schedule. How the committee will view the receipt of the five letters of intention, as an index of European interest in the total program, is yet to be seen. A critical test will come in September when definite, obligated projects, rather than letters of intention, will be called for by the Euratom administrators.

National Science Foundation's Budget Cut by House

The House of Representatives cut $17 million from the National Science Foundation's requested budget of $160 million for fiscal year 1960. The cut, which may be partially restored by the Senate, leaves the foundation with $143 million—an insufficient amount, according to the director, Alan T. Waterman, to ensure adequate government support for basic scientific research. The foundation had originally requested $206 million, but the Bureau of the Budget lopped off $46 million in line with the Administration's balanced-budget policy.

On the House floor almost no debate followed the introduction of the Appropriations Committee recommendations, and no member of the House urged that the sizable cut be restored. The members simply approved the committee's action. Apparently, there was general agreement with Representative Joe L. Evins (D-Tenn.) of the Appropriations Committee when he said, "The committee is impressed by the importance of science in the modern world, but it does not believe we should issue a blank check to the Foundation. An increase of $9 million over the funds provided last year should provide a substantial increase in NSF activities."

The House cut left some programs of the foundation intact, with appropriations at the level deemed necessary by NSF officials. Among the programs that might have to be curtailed if the cuts remain, according to Waterman, are research studies on weather modification, plans to continue and enlarge programs for translating Russian scientific works, and proposals to support a larger percentage of the research projects that are submitted to the foundation each year. The effect of the cut will be particularly serious in this last area, foundation officials say. The $60.5 million approved by the House for these basic research grants is, according to the director, "inadequate to meet the Foundation's objective."

Other House Action

In other budgetary developments, the same House Appropriations Committee approved $17.25 million for research and technical services at the National Bureau of Standards. This is an increase of about $5 million over last year's authorization. These funds will allow the bureau to buy six new field stations that are now operated under lease and to build another wing at its Boulder, Colo., station.

Another division of the Commerce Department, the Weather Bureau, received $49.85 million from the House committee to support its activities in fiscal 1960. Last year's figure was $45.24 million. These funds were authorized with the stipulation that 24-hour weather station operations at major airports be restored. During the past two years the bureau has had to cut down on weather services at 51 airports around the country. With the funds authorized by the committee, around-the-clock service will be resumed at 13 of these stations.

The House's action on these budgetary matters is only the first round for the various federal agencies involved. The cuts and the increases must be passed on by the Senate, and the actions of House and Senate, if different, must be reconciled before the final money authorizations are made. In its appropriations for science and technology the Senate tends to be a little more generous than the House. Because there has been no particular criticism of the House action by members of the Senate, there is reason to believe that there will be no drastic revisions of the various appropriations when the Senate acts.

Australian Academy of Science

Scientists in various fields of international scientific endeavor will have observed that Australia has been represented by the Australian Academy of Science in arrangements for participation in the International Geophysical Year, for the Symposium on the Chemistry of Natural Products in Australia in 1960, for the specialist Conference on Haematin Enzymes in September 1959, and for activities of the Pacific Science Association and Pan Indian Ocean Science Association.

The Australian Academy of Science is a relatively recent establishment. Prior to 1954 Australian science had been represented in international activities by the Australian National Research Council. This council, which was formed in 1919, particularly to provide for Australia's participation in the International Research Council, acted for many years as the top representative body of science in Australia. Many Americans will recall the activities of the council, perhaps chiefly in connection with its participation in Pacific Science Association affairs and for its long and successful program of anthropological research.

Over the years the National Research Council had widened its membership to include leaders in the social sciences as well as in the natural sciences. By 1951 there was a strong feeling that the natural sciences needed a body of men, distinguished in their respective fields, to foster the pursuit of the natural sciences in Australia and to represent Australia in the increasing international activities. The social scientists were also ready to form a separate organization, now known as the Social Science Research Council.

The Australian National Research Council agreed to the suggestion that two entirely new bodies should be formed and that the old Research Council should be disbanded. The initiative in the natural sciences was taken by a group of 12 fellows of the Royal Society of London, resident in Australia, who invited 11 other scientists of high standing to join them. These scientists became the Foundation Fellows of the Australian Academy of Science and received a sympathetic hearing from the Prime Minister, the Right Honorable R. G. Menzies, who promised financial support

The new Australian Academy of Science Building in Canberra.

to launch a vigorous academy. With the help of the Australian Government and the Royal Society of London, the group of founders obtained a Royal Charter which established the Australian Academy of Science as a body with proper legal status and adequate prestige. In the early part of 1954 Her Majesty Queen Elizabeth II visited Australia and was graciously pleased to present her charter to the provisional council of the academy at a simple ceremony at Government House, Canberra, on 16 February 1954, thus following the precedent of King Charles II, who presented his charter to the Royal Society of London in 1662.

The charter required that the academy should be enlarged to at least 50 fellows within 3 months. Six fellows, distinguished for their achievements in the natural sciences, are elected annually, and the total fellowship is now 81.

The first task of the academy was to take over, from the National Research Council, Australia's representation in international scientific affairs. An early duty was the organization of Australia's participation in IGY and, as an indication of the confidence in the young academy, the necessary grant from the Australian Government was provided. The coordination of Australia's scientific resources for IGY was placed in the hands of a national committee and carried out on an honorary part-time basis.

The academy has a general policy of supporting other Australian scientific bodies, such as the professional bodies. The question of an academy publication was considered, but it was decided to support existing publications rather than to start a new one. In particular, there is a group of eight journals—for example, the *Australian Journal of Physics*—whose scientific direction is in the hands of a Board of Standards appointed jointly by the CSIRO (Commonwealth Scientific and Industrial Research Organization) and the Academy of Science.

Not all the activities of the Australian Academy of Science can be listed here. The academy continues to have the confidence of the Australian Government and is consulted on questions of scientific policy. Like its counterpart in the United States, the academy has its headquarters in the national capital. A new building to house the academy, in contemporary (and, in some quarters, controversial) design was opened in May.

J. DEEBLE

Australian Academy of Science, Canberra

Engineering Enrollment Falls, Teachers' Salaries Rise

Freshman engineering enrollment has declined markedly for the first time in 8 years. Furthermore, one out of five engineering schools expects a further drop in freshman enrollment next fall. In 1958, 70,029 engineering freshmen enrolled in the nation's schools, as compared with 78,757 in 1957, a drop of 11.1 percent. However, total college freshman enrollment in this country continued to increase, having risen nearly 7 percent over the previous year.

These facts were announced recently by the Engineers Joint Council, which reported on a special survey of its Engineering Manpower Commission that had been conducted in cooperation with the American Society for Engineering Education. The study, *Trends in Freshman Engineering Enrollment*, covered 223 institutions in the United States that grant degrees in engineering.

According to the heads of the engineering schools, applications of qualified students fell for three reasons: (i) because of a false appraisal of the long-range engineering career opportunities on the part of counselors, students, and parents, based on reports in the general press on reduction of company engineering complements during the 1957–58 recession period; (ii) because of increased concern about rigors of the engineering curriculum; and (iii) because of increased interest of potential engineering students in other scientific fields resulting in diversion of students to other educational pursuits.

The Engineering Manpower Commission survey was under the direction of a four-man committee, which included H. H. Armsby, chief for engineering education, Office of Education, U.S. Department of Health, Education and Welfare; D. S. Bridgeman, consultant Engineering Manpower Commission; R. W. Cain, project director, Scientific Manpower Studies, National Science Foundation; and L. K. Wheelock, executive secretary, Engineering Manpower Commission.

Teacher's Income Studied

Another recent study by the Engineers Joint Council shows that the average professional income of engineering teachers in the United States has risen 8.3 percent since 1956 and their basic teaching salaries have increased 13.5 percent over the 2-year period. The survey covered more than 5000 engineering teachers, or about half of the teachers in this field in the United States.

By the nature of their occupation, engineering teachers must do research; therefore, they earn more than basic teaching salaries. Thus, the average total professional income of engineering teachers, which was $8862 in 1956, was $9598 in 1958. The basic salary average rose by $894 per year, but there was a decline of 7 percent in outside income. For deans and department heads, however, there was an increase in both teaching and outside income.

The total income of engineering teachers in public institutions rose more than the total income of those in privately supported institutions. Engineering teachers holding advanced degrees earned more. In general, the survey

showed that the teaching salaries of engineering educators increase with age. These basic salaries ranged from a low of $6744 in the South to $8392 in the Pacific region.

The report, entitled *Salaries and Income of Engineering Teachers, 1958,* was published by the Engineers Joint Council as a supplement to a recent report, *Professional Income of Engineers —1958,* and was prepared by the Bureau of Business and Economic Research at Northwestern University, Boston. Copies are available from the Engineers Joint Council, 29 W. 39 St., New York 18, N.Y., at 25 cents to cover handling cost.

Scientific Manpower in Government

Attractive features found only in government scientific and technical programs must be emphasized if federal agencies are to be more successful in attracting and retaining their required share of first-rate scientists and engineers. This advice to federal officials was underscored by several prominent scientists, engineers, and personnel officials in speeches to the 2-day government-wide Conference on Scientific Manpower, held recently in Washington, D.C. Some 500 federal officials and others concerned with government scientific staffing attended the conference, which was sponsored by the U.S. Civil Service Commission, with the Office of Naval Research as host agency.

The conference was arranged to consider solutions to the problem of insuring the maintenance of highly competent research and development staffs in federal laboratories. The speakers included James R. Killian, Jr., special assistant to the President for science and technology; A. B. Kinzel, vice president for research, Union Carbide Corporation; Roger W. Jones, chairman of the Civil Service Commission; Rocco C. Siciliano, special assistant to the president for personnel management; Guy Suits, vice president and director of research, General Electric Company; Ralph D. Bennett, manager of the General Electric Company's Vallecitos Atomic Laboratory in California; John G. Darley, associate dean and head of the department of psychology, University of Minnesota; and Harry C. Kelly, assistant director for scientific personnel and education, National Science Foundation.

Conference participants emphasized the following points.

Competition for superior scientific personnel can be expected to continue, and possibly to be intensified in the foreseeable future.

It is unlikely that government compensation for scientists and engineers can be made fully competitive with pay offered by industry, but the gap can in large part be offset by other attractions which only the federal service can offer.

The solution to the pay problem requires more flexibility in the Government's pay structure rather than a separate pay system for scientists and engineers. Federal scientists already receive many of the benefits they seek, but agencies need to make them more aware of this fact.

The Government's career scientific service must be flexible enough to allow for advancement to top levels for scientists who wish to stay in creative work rather than transfer to administration.

The Government must recognize that scientists have different interests and motivation from nonscientists, which require special consideration, and agencies must develop attractions that interest them.

The popular image of the scientist must be improved.

Undue reliance on outside laboratories for new work of large scientific interest could greatly impair the morale of government scientists and the vitality of needed public facilities.

The Government has shown marked improvement in the recruiting of scientists and engineers in the past 2 years.

One of the most important challenges to the Government is the need to correct erroneous concepts of public service.

Speakers from industry, government, and universities stressed the point that federal scientific and technical programs offer unusual and challenging opportunities which exist nowhere else, and that the Government should take steps to point up the many areas in which it offers superior attractions. Among the benefits of the Government's career scientific service cited were the opportunity to conduct research on a wide variety of exciting and challenging programs; to engage in basic research without production-related pressures; to work in the most modern and fully equipped facilities without worry about the adequacy of research funds; to participate in pioneering work in new areas of science and technology; to publish research results without fear of compromising the employer's competitive position; to gain public recognition of professional achievements; and, finally, to participate in work that is important to national security and progress.

Expedition Monsoon

During the months of February to August 1960 two ships of the University of California's Scripps Institution of Oceanography will engage in a deep-sea expedition to the western Pacific and eastern Indian Ocean. The expedition, tentatively called Monsoon, will be similar to the 1952–53 Capricorn and 1957–58 Downwind investigations of the south and southeast Pacific. The ships, separately and together, will carry out bathymetric, sonoprobe, seismic-refraction, magnetic, heat-flow, bottom-sampling, bottom-photographic, hydrographic, and gravity reconnaissance studies of the western Pacific, part of the East Indian Archipelago, and the eastern part of the Indian Ocean. Measurements of carbon dioxide in the atmosphere and near-surface water will be made throughout the cruise. Large-volume water sampling and radioisotope and trace element studies will be carried out, especially in the north Pacific and Indian Ocean segments. The biological program will consist of plankton sampling throughout the cruise and of mid-water trawls and dredging for benthic organisms in the equatorial Pacific, East Indies, and eastern Indian Ocean.

As in the case of the Downwind cruise, there will be two expedition leaders. Henry W. Menard will supervise the East Indies-Indian Ocean operations; Robert L. Fisher will direct the ships' operations in the Philippine, Japanese, and Kuril areas.

NIH Grants Division Reorganized

The 31 study sections of the Division of Research Grants at the National Institutes of Health have recently been divided into four research groups for review of research grant applications. These review panels are comprised primarily of nongovernment scientists who have also the added responsibility of surveying the status of research in their respective fields and making recommendations to the Public Health Service as to what additional activity should be undertaken. The new administrative structure will enable the four research groups, operating under the Research Grants Review Branch of the Division of Research Grants, to expedite the large volume of research grant applications and at the same time to maintain a high quality of professional review.

The head of each group will coordinate the activities of his study sections and serve as project review officer for applications falling within the province of his group. The four research groups and their respective scientist-administrators are as follows: (i) clinical research, Clinton C. Powell, formerly executive secretary of the radiation and surgery study sections; (ii) biochemistry and physical science, Elsa O. Keiles, formerly executive secretary of the metabolism and nutrition study section; (iii) biological sciences, J. Palmer

Saunders, formerly executive secretary of the cancer chemotherapy study section; and (iv) health services, Murray Goldstein, formerly assistant chief of the grants and training branch, National Heart Institute.

Science and Public Policy Program Continued at Harvard

Harvard University has announced the receipt of a grant of $285,000 from the Rockefeller Foundation to continue the support of a research and training program in science and public policy that was started last year by the Graduate School of Public Administration. The program, which will extend through 1962–63, is investigating the broad range of problems involved in the financing and administration of scientific research and in the application of science to the formulation and determination of public policy.

Beginning in the autumn of 1960, the program will also undertake to train a number of scientists and administrators who are actively concerned with these problems. At that time, a group of 15 fellows will be admitted for graduate study. These students will be selected primarily from among candidates who have had a number of years of experience in Government or in research positions and who seek to prepare themselves to deal with public-policy issues at a higher level of responsibility. Such students may qualify for the master of public administration degree in one academic year.

Associated in the conduct of the program are four Harvard professors: Jerome S. Bruner, professor of social relations; I. Bernard Cohen, professor of the history of science; Carl Kaysen, professor of economics; and Don K. Price, professor of government and dean, Graduate School of Public Administration.

Transcontinental Radio Link

By using a large balloon, about 1000 miles out in space, the National Aeronautics and Space Administration plans to establish a transcontinental radio link late this year. The new project, which is said to be in an advanced stage of development, will relay radio signals between California and New Jersey by bouncing them off the aluminized skin of a balloon, 100 feet in diameter, which will be put into orbit by a rocket.

As the satellite, during its travels from 50° north to 50° south latitude, passes over the United States, radio signals will be directed toward it. After reflection, these signals will be picked up by receivers in either New Jersey or California, depending on the direction of transmission. The California facilities will be located at Goldstone, where there is an 80-foot antenna that has been used in the past for space communications.

The relay project is the first step in the Space Administration's long-range plan to establish a new global system for relaying radio messages, telephone calls, and television programs between continents. It also may represent, in the opinion of NASA officials, a means of breaking the potential log jam that is developing in conventional communication channels.

Congress Gets NATO Atom Pacts

Agreements by which four NATO countries would be given help in training their troops in the use of atomic weapons were sent to Congress last month. Under the pacts, military units in West Germany, the Netherlands, Turkey, and Canada would receive the necessary training, equipment, and information for use of nuclear weapons in defense operations. In line with amendments of the Atomic Energy Act adopted last year, the nuclear warheads would remain under the control of U.S. forces. The agreements, which were approved by the four NATO countries last month, will become effective 60 days after submission unless the Congress disapproves them by a concurrent, or combined, House and Senate resolution.

Western Commission for Higher Education Formed

More than 40 graduate deans from Western universities and colleges have approved a constitution outlining the functions and organization of the Western Association of Graduate Schools. A meeting of the deans has indicated that almost all of the Western colleges and universities giving graduate degrees will become members of WAGS.

Officers of the new organization are deans Herbert D. Rhodes (University of Arizona), chairman; Luther J. Lee, Jr. (Claremont Graduate School), chairman-elect; and Dayton D. McKean (University of Colorado), secretary-treasurer. These three men and deans Stewart E. Hazlet of the State College of Washington and Robert W. Hiatt of the University of Hawaii form the executive committee for the association. All graduate schools at public and private universities in the following states are eligible to apply for membership: Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming.

Science Study Series

In September 1959, the first of a series of paperbacks devoted to the popular presentation of physics will be published. The series, which will have the Doubleday Anchor Books format, had its origin in the work of the Physical Science Study Committee, an educational group formed at the Massachusetts Institute of Technology in 1956. The committee is currently completing a final version of a new physics textbook (which is being used this year by 13,000 high-school seniors on a trial basis) and producing a series of classroom films.

The series of paperbacks (to be called the Science Study Series) was originally conceived of as supplementary reading for use in connection with the textbook and films, but it was later decided to make the books available to the general public. The first of the series to appear will be *The Neutron Story*, by Donald J. Hughes; *Magnets*, by Francis Bitter; *Soap Bubbles and the Forces Which Mould Them*, by C. V. Boys; *Echoes of Bats and Men*, by Donald R. Griffin; and *How Old is the Earth?* by Patrick M. Hurley.

International List of Translations

The United Nations Educational, Scientific, and Cultural Organization has published the 10th volume of *Index Translationum*, an international bibliography which lists 27,978 titles of books issued in translation from 65 countries in more than 200 languages. The annual compilation covers the year 1957, but some earlier works not previously listed are also included. The translations are grouped by countries in fields such as philosophy; religion and theology; law, social sciences, and education; philology and linguistics; natural and exact sciences; applied sciences; arts, games, and sports; literature; history, geography, and biography.

A tabulation according to subject and country shows that literary works, especially novels, account for more than half the translations (15,407). The U.S.S.R., as in previous years, holds the record for countries in the number of translations listed, with 4608, in all languages of the Soviet Union, in addition to some translations in Spanish and English. Of these, 700 are scientific works. Next comes Germany (including the Federal Republic and the Democratic Republic) with 2041, followed by France, Japan, Italy, Czechoslovakia, the Netherlands, Sweden, and Romania, with more than 1000 translations each. *Index Translationum* is available at the Unesco Publications Center, 801 3rd Ave., New York, (cloth, $20; paper, $18).

Canadian Mapping Program

More than 1000 men, comprising 81 individual field survey parties, will conduct the annual mapping and charting program this year for the Surveys and Mapping Branch of the Canadian Department of Mines and Technical Surveys.

The program, which is getting under way now and will continue through November, will take survey parties to all ten Canadian provinces as well as into the Yukon and the Northwest Territories and into navigable coastal and inland waters. Included in the field survey force will be 28 units of the Canadian Hydrographic Service.

In announcing the program, Mines Minister Paul Comtois stated that increasing emphasis is being placed on the development of Canada's northland.

The over-all program has a twofold objective. The long-range purpose is to provide data for the preparation of base maps and charts of various scales, covering the entire Dominion; the short-range objective is to stimulate the development of areas of potential resources, such as minerals, water power, and forests. Defense needs are also a factor in the mapping and charting program.

Grants, Fellowships, and Awards

Arthritis and rheumatism. The Arthritis and Rheumatism Foundation offers predoctoral, postdoctoral, and senior investigatorship awards in the fundamental sciences related to arthritis for work beginning 1 July 1960. Deadline for applications is *31 October*.

These awards are intended for fellowships to advance the training of young men and women of promise for an investigative or teaching career. They are not in the nature of a grant-in-aid in support of a research project. The program provides for three types of award.

Predoctoral fellowships are limited to students who hold a bachelor's degree. Each applicant studying for an advanced degree must be acceptable to the individual under whom the work will be done. These fellowships are tenable for 1 year, with prospects of renewal. Stipends range from $1500 to $3000 per year, depending upon the family responsibilities of the fellow.

Postdoctoral fellowships are limited to applicants with the degree of doctor of medicine, doctor of philosophy, or their equivalent. These fellowships are tenable for 1 year, with prospect of renewal. Stipends range from $4000 to $6000 per year, depending upon the family responsibilities of the fellow.

Senior investigator awards are made to candidates holding, or eligible for, a faculty rank, such as instructor or assistant professor (or equivalent) and who are sponsored by their institution. Stipends are from $6000 to $10,000 per year and are tenable for 5 years.

A sum of $500 will be paid to cover the laboratory expenses of each postdoctoral fellow and senior investigator. An equal sum will be paid to either cover the tuition expenses or laboratory expenses of each predoctoral fellow. For further information and application forms, address the Medical Director, Arthritis and Rheumatism Foundation, 10 Columbus Circle, New York 19, N.Y.

Cardiological research. Applications are now being accepted by the American Heart Association for support of research to be conducted during the fiscal year beginning 1 July 1960. The deadline for applying for research fellowships and established investigatorships is *15 September*. Applications for grants-in-aid must be made *by 1 November*.

Support is given not only to studies with a direct bearing on problems of cardiovascular medicine but also to basic research in a wide range of scientific disciplines. The association recently announced its national awards for the 1959–60 fiscal year, representing an allocation of approximately $3,300,000.

Established investigatorships are awarded for periods of up to 5 years, subject to annual review, in amounts ranging from $6500 to $8500 yearly, plus dependency allowances, to scientists of proven ability who have developed in their research careers to the point where they are independent investigators. In addition, a grant of $500 is made to the investigator's department. Applicants for established investigatorships may apply for grants-in-aids to support their research at the same time they apply for established investigatorships.

Advanced research fellowships are awarded for periods of 1 or 2 years to postdoctoral applicants who have had some research training and experience but who are not clearly qualified to conduct their own independent research. During the second year of tenure they will be permitted to spend up to 25 percent of their time in professional and scientific activities not strictly of a research nature, provided that these will contribute to their professional development and do not involve services for a fee. These stipends range from $4600 to $6500 annually. Additionally, a grant of $500 is made to the investigator's department, as in the case of established investigators.

Research fellowships are available to a limited number of young men and women with doctoral degrees for periods of 1 or 2 years to enable them to train as investigators under experienced supervision. Annual stipends range from $3800 to $5700.

Grants-in-aid are made to experienced investigators to help underwrite the costs of specified projects, such as equipment, technical assistance, and supplies.

Further information and application forms may be obtained from the Assistant Medical Director for Research, American Heart Association, 44 E. 23rd St., New York 10, N.Y.

Radioisotope technology. The Atomic Energy Commission has announced approval of grants totaling $251,704 to 12 American colleges and universities. The grants are a part of the commission's new program of assistance for education and training in radioisotope principles and technology. Detailed information on the program and instructions for the submission of proposals may be obtained by writing to the Director, Office of Isotopes Development, U.S. Atomic Energy Commission, Washington 25, D.C.

Science writing. The Arthritis and Rheumatism Foundation has announced that the Russell L. Cecil Award for science writing will in 1959, for the first time, include an honorarium of $500. The honorarium will also be included in future awards. The award was established in 1956 to encourage the writing of stories and scripts on arthritis for general circulation newspapers, magazines, and the broadcasting media. All entries must be submitted by *31 January 1960*. Further information is available from the Arthritis and Rheumatism Foundation, 10 Columbus Circle, New York 19, N.Y.

Social science. The Office of Social Sciences of the National Science Foundation has announced that the next closing date for receipt of basic research proposals in the social sciences is *1 October*. Proposals received prior to that date will be reviewed at the fall meeting of the foundation's advisory panel and disposition will be made approximately 4 months following the closing date. Approved grants will be activated in time for work to begin in the second semester or summer of 1960. The Office of Social Sciences supports basic research in anthropology, archeology, demography, human ecology, sociology, social psychology, economics, economic and social geography, and the history and philosophy of science.

Proposals received after the 1 October closing date will be reviewed following the closing date of 1 February 1960, with activation of approved grants in the summer and fall of 1960. Inquiries should be addressed to the National Science Foundation, Washington 25, D.C.

News Briefs

The Josiah Macy, Jr. Foundation recently awarded unrestricted grants of $50,000 per annum for a 3-year period to each of 11 private medical schools for

strengthening their research-teaching staff, particularly in the medical science departments. This interim assistance will help a few private medical schools during the period in which efforts are being made to secure support of a permanent character. These grants, totaling $1,650,000, were made by the foundation in recognition of the fact that at present there are more funds for medical research than there are facilities and permanent staff to carry out the programs.

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A new department of virology has been established on the Berkeley campus of the University of California. This is one of the first departments in any major university to be dedicated to the study of viruses; it will be closely associated with the 10-year-old Virus Laboratory at Berkeley. Chairman of the new department is Wendell M. Stanley, Nobel laureate and director of the Virus Laboratory. Eight faculty members, drawn from the Virus Laboratory, now comprise the staff of the department.

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A 64-page International Geophysical Year bibliography that lists 704 references on the IGY published between January 1951 and August 1958 may be obtained for $1 from the National Academy of Sciences, Washington 25, D.C. Entries in *An Interim Bibliography on the International Geophysical Year* were selected for scientific value, extent of coverage, historical interest, uniqueness, and availability. English translations are given for titles in Russian, East European languages, and Japanese, and the availability of complete translations or English summaries is noted.

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The International Atomic Energy Agency, Vienna, Austria, has released the first issue (a 20-page pamphlet) of a chronological list of atomic energy conferences, meetings, and training courses.

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In Canada the president of the National Research Council and the chairman of the Defence Research Board are in the process of establishing a Permanent Joint Committee on Space Research. Canadian governmental agencies concerned with these matters, and a number of interested universities, will have representatives on the committee.

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Sixty-nine corporations are now matching the gifts their employees make to colleges and universities, according to the American Alumni Council (Washington, D.C.). Four years ago the General Electric Company pioneered in this approach to business support of colleges and universities by introducing the Corporate Alumnus Program. For every gift which General Electric personnel made to institutions of higher learning from which they held degrees, the company contributed a like amount. Since the start of the program in 1955, more than $800,000 has been distributed to match the gifts of General Electric employee-alumni.

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A group of specialists in nuclear medicine have formed Medical Nuclear Consultants, Inc., with headquarters in Washington, D.C. (5506 Connecticut Ave., NW) and offices in New York and Montreal. Services will be made available to sponsors of diagnostic, treatment, and research programs, according to Stanley H. Clark, radiation physicist and president of the group. He was formerly in charge of radiation protection for the General Electric Research Laboratories in Schenectady, N.Y.

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The Report of the U.S. Public Health Mission to the Union of Soviet Socialist Republics, Public Health Service Publication No. 649, contains the findings of a mission of five doctors who visited the Soviet Union late in 1957 under the exchange program approved by the two countries in 1956. Members of the mission traveled 8500 miles and visited 61 institutions in nine cities in five of the Soviet republics during August and September 1957.

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The American Association of Physics Teachers has released a report on the sizes of lecture rooms used in 430 physics departments in the United States. Based on a postcard questionnaire sent by an AAPT committee to 540 departments which offer a major in physics, the one-page report contains information that will be of interest to designers and manufacturers of lecture-room equipment.

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A limited number of well-known neurobiologists are being invited to attend a meeting to be held next September on the occasion of the 50th anniversary of the Netherlands Central Institute for Brain Research at Amsterdam. This congress is also to pay homage to the memory of C. U. Ariëns Kappers, the institute's first director.

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In behalf of the Histochemical Society the editorial office of the *Journal of Histochemistry and Cytochemistry* maintains a register of positions and personnel available in the field of histochemistry. Inquiries may be directed to Dr. J. B. Longley, National Institutes of Health, Bethesda, Md. A fuller statement of the principles on which the register is operated appeared on the January 1959 issue of the *Journal.*

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A new journal of statistics for the physical, chemical, and engineering sciences has been started by the American Society for Quality Control and the American Statistical Association. Entitled *Technometrics,* the new publication is edited by J. Stuart Hunter at Princeton University. *Technometrics* will be issued quarterly in February, May, August, and November. For information, write to the American Statistical Association, Room 404, Beacon Building, 1757 K St., NW, Washington 6, D.C.

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Three of the U.S. Atomic Energy Commission's traveling exhibits will be presented at some 50 colleges and universities in ten states during the summer months in a new "Atoms at Work" science-teacher training program. The National Science Foundation has made funds available to help support the program, which will be administered by the Museum Division of the Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tenn., in cooperation with the National University Extension Association.

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The American Heart Association has announced that it will spend a total of approximately $3,300,000 for scientific studies in the field of heart and blood-vessel diseases during the 12 months beginning 1 July. This is the largest sum ever appropriated by the association to support research in a single fiscal year and represents a commitment of approximately 57 percent of the income received from public contributions to last year's Heart Fund appeal.

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In a report issued last month, the National Education Association urged that instruction in geography in the country's schools be modernized and restored to the curriculum as the unified subject it once was. The report, titled, "New Viewpoints in Geography," cited the many changes, both in factual material and in methods of instruction, that had taken place. Physical and economic geography are fields in which new and better instruction would be of particular value, the report noted.

* * *

The Atomic Energy Commission will close its uranium mill at Monticello, Utah, on or about 1 Jan. 1960. This mill, the only commission-owned uranium ore processing plant, will be maintained in a stand-by condition. The Monticello mill is being operated by National Lead Company, Inc., under an AEC contract. With the closing of the Monticello mill, all domestic ore processing will be carried on by private industry. Twenty-two privately owned mills are in operation throughout the Western states.

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The Committee on the International Exchange of Persons at the National Academy of Sciences–National Research Council has compiled a new list of for-

eign scholars available for remunerative positions in American universities and colleges during the academic year 1959–60. This 11-page list, which is distributed on request, is prepared annually and includes scholars recommended by the United States educational commissions and foundations abroad. Each scholar on the list is eligible for a government travel grant covering round-trip transportation to the United States if arrangements are made for a lecturing or research appointment.

Scientists in the News

A. OLIVER, director of the New York Zoological Park, has been appointed director of the American Museum of Natural History. He succeeds ALBERT E. PARR, director since 1942, who has been appointed senior scientist of the museum in accordance with a policy recently adopted by the board of trustees that enables a director to resume full-time research after 15 years of administrative service. JOHN TEE-VAN, general director of the New York Zoological Park and the New York Aquarium, will again assume full directorship of the zoo on 15 September. He was director from 1952 to 1956.

Parr, a distinguished marine biologist, was graduated from the Royal University of Oslo and served with the Bergen Museum and the Norwegian Bureau of Fisheries before leaving Norway for the United States in 1926. His first major appointment in this country was in 1927, when he became curator of the Bingham Oceanographic Collection. He joined the American Museum from Yale University, where he had served successively as professor of oceanography, director of oceanic expeditions, and director of the Peabody Museum of Natural History. He has received two honorary D.Sc. degrees, one from Yale University and one from Colby College.

At the American Museum, Parr's 17-year administration has been notable for the establishment of an optimum climate for research and scholarship, for the development of a new philosophy of exhibition, and for pioneering techniques of interpretation. The Warburg Memorial Hall of Ecology is the embodiment of Parr's philosophy of teaching the interrelationships of all living organisms. Ten major exhibition halls were completed under his direction.

ANTHONY J. DE LORENZO, former faculty member of the Washington University School of Medicine (St. Louis), has been appointed director of the Anatomical and Pathological Research Laboratory in the department of otolaryngology at the Johns Hopkins University School of Medicine. He succeeds STACY R. GUILD, who has retired after 33 years as director. De Lorenzo also is assistant professor in the department of anatomy.

WILLIAM M. HESTON, JR., of the employee relations department at E. I. duPont de Nemours & Company, Wilmington, Del., has been appointed by Western Reserve University to the newly established position of director, office of university research, and associate in the department of chemistry, effective 1 July. He will assist faculty members in preparing requests for research grants, will review all research budgets, and will supervise the reporting and accounting of research money.

WILLIAM J. PYLES, assistant clinical professor of medicine at Columbia University College of Physicians and Surgeons, has been appointed medical director of the New York Heart Association. He succeeds D. F. MILAM, who retired 1 June.

ERWIN L. JUNGHERR, professor of animal pathology and head of the department of animal diseases, University of Connecticut, will retire on 1 July. He expects to join the virus and rickettsial research staff of Lederle Laboratories, American Cyanamid Company, Pearl River, N.Y.

KARL SCHWARTZWALDER, director of research at the AC Spark Plug Division of General Motors, in Flint, Mich., has recently received the John Jeppson Medal of the American Ceramic Society.

MAX T. WEISS, specialist on microwave physics at Bell Telephone Laboratories for 9 years, has joined Hughes Aircraft Company as senior staff physicist of the microwave laboratory's electronics research department.

FRED W. DROSTEN, former reactor engineer with the U.S. Atomic Energy Commission's Oak Ridge Operations Office, has been named director of metallurgical development for the Heavy Minerals Company, a subsidiary of Vitro Corporation of America.

JOHN STERNER has resigned as director of flight test operations for Space Technology Laboratories at Cape Canaveral, Fla., to join with WILLIAM P. MURPHY, JR., research associate professor at the Miami School of Medicine, in founding the Cordis Corporation in Miami, Fla., a medical instrument firm. Murphy will be the new corporation's president, and Sterner will be vice president.

ROBERT W. NOYES, associate professor of obstetrics and gynecology at Stanford University Medical School, and THOMAS H. CLEWE and AILEEN YAMATE, research associates, have received the Rubin Award of the American Society for the Study of Sterility for their work on ovarian transplants to the anterior chamber of the eye.

CARROLL L. ZIMMERMAN, chief scientist for the Strategic Air Command, Offutt Air Force Base, Neb., has been appointed director of the operations analysis office at the U.S. Air Force headquarters in Washington, D.C.

CECIL P. HEADLEE, professor of pharmacology and physiology at Northeastern Louisiana State College School of Pharmacy, has been appointed scientific director at the C. B. Kendall Company, Indianapolis, Ind.

DAVID H. NEWBY, formerly chief of the test and evaluation laboratory, U.S. Army Ordnance Corps, Huntsville, Ala., has been appointed representative of the National Aeronautics and Space Administration at the Army Ordnance Missile Command, Huntsville, Ala.

FRANK F. DARLING, formerly senior lecturer in ecology and conservation at the University of Edinburgh, Scotland, has been appointed vice president of research at the Conservation Foundation, New York. Darling has been a member of the foundation's scientific advisory council for many years.

NORMAN KHARASCH, professor of chemistry at the University of Southern California, has been awarded a Fulbright research grant to spend the 1959–60 academic year in Austria at the Vienna Institute of Technology.

JAMES McCONNELL, professor at St. Patrick's College, Maynooth, Ireland, will spend the 1959–60 academic year as visiting professor of physics at Fordham University, where he will lecture on field theory and fundamental particle physics.

FREDERICK REINES, group leader at the Los Alamos Scientific Laboratory, has been appointed professor and head of the physics department at Case Institute of Technology, effective 1 July.

FREDERICK J. GUTTER, chemist in the laboratory of biochemistry at the National Cancer Institute, has been transferred to the extramural programs branch of the National Institute of Neurological Diseases and Blindness, National Institutes of Health, Bethesda, Md.

ARNOLD B. GROBMAN, associate professor of biology at the University of Florida, and director of the Florida State Museum, will be on leave of absence from both positions to head the American Institute of Biological Sciences study group on biological sciences curricula. The study group, which has headquarters at the University of Colorado, Boulder, will spend two to three years developing curricula, for high schools and junior colleges in particular, but for educational institutions at other levels as well.

LORUS J. MILNE, professor of zoology at the University of New Hampshire, and his wife, Dr. Margery Milne, have been invited to the Union of South Africa to serve during the summer of 1959 as visiting lecturers in the biological sciences. They will also discuss research on invertebrate vision in the nine universities of the Union and will visit the headquarters of the Institute for Scientific Research in the Belgian Congo.

BORJE UVNAS, professor of pharmacology, Karolinska Institutet, Stockholm, Sweden, recently served as lecturer in physiology at the University of California School of Medicine, Los Angeles. He discussed his current research on gastric secretion, vasomotor mechanisms, and mast-cell disruption.

W. F. G. SWANN, internationally known physicist and director of the Bartol Research Foundation of the Franklin Institute for 32 years, will retire and become director emeritus on 1 September. MARTIN A. POMERANTZ, senior staff physicist at Bartol, will succeed Swann, who will continue his research at the foundation and serve as a special consultant to staff members.

Swann, who is a native of England, received his doctor of science degree from London University in 1910. He came to the United States in 1913 as chief of the physical division of the department of terrestrial magnetism at the Carnegie Institution in Washington, D.C. He was appointed professor of physics at the University of Minnesota in 1918 and professor of physics at the University of Chicago in 1923. In 1924, he became professor of physics and director of the Sloane Laboratory at Yale University, where he served until 1927, when he became the first director of the foundation.

Swann is the author of two books, *The Architecture of the Universe* and *Physics*, and coauthor of *The Story of Human Error*. He is noted for his work in the fields of atmospheric electricity, cosmic radiation, accurate thermal measurements, electrodynamics, relativity, and quantum theory.

WILLIAM W. HAMBLETON, associate director of the State Geological Survey and associate professor of geology at the University of Kansas, will be on sabbatical leave for the 1959–60 academic year to perform geophysical research at Columbia University's Lamont Geological Observatory. PAUL C. FRANKS will be acting assistant director of the State Geological Survey.

JONATHAN E. RHOADS, provost of the University of Pennsylvania, will resign from that position and devote himself to the practice of surgery and to the posts of professor of surgery in both the School of Medicine and the Graduate School of Medicine, and of assistant director of the Harrison department of medical research at the university.

ALBERT E. NAVEZ, chairman of science education for the Newton (Mass.) public schools, and RAYMOND SCOTT, head of the science department at Rindge Technical High School, Cambridge, Mass., have received the Elizabeth Thompson awards for the advancement of science education of the American Academy of Arts and Sciences.

ALVIN C. EURICH, executive director, Education Division of the Ford Foundation, and vice president of the Fund for the Advancement of Education, has been appointed chairman of the Commission on Health Careers. The commission was established more than a year ago by the National Health Council, to join with the health professions, and agencies, in efforts to reduce the health manpower shortage.

FRANK K. SCHOENFELD, vice president of research and development of the B.F. Goodrich Company, Akron, Ohio, has received the Industrial Research Institute Medal for outstanding accomplishment in "leadership in or management of industrial research which contributes broadly to the development of industry or the public welfare."

MILTON B. AMES, JR., chief of the Aerodynamics and Flight Mechanics Division of the National Aeronautics and Space Administration, has been appointed director of aeronautical and space research (aeronautics and flight mechanics). He succeeds IRA H. ABBOTT, who recently was named deputy director of Aeronautical and Space Research.

MARSHALL F. CROUCH, associate professor of physics at Case Institute of Technology, has been appointed by the State Department to serve for 2 years as scientific attaché at the American Embassy in Tokyo, Japan.

J. A. POPLE, superintendent of the Basic Physics Division, National Physical Laboratory, Teddington, England, is in the United States and plans to attend the Gordon Research Conference session on magnetic resonance, New Hampton, N.H., 6–10 July.

JOSEPH V. CHARYK, chief scientist of the Air Force, has been appointed assistant secretary of the Air Force. He succeeds RICHARD C. HORNER, who has been appointed associate administrator of the National Aeronautics and Space Administration.

HAROLD F. DORN, chief of the biometrics branch of the Division of Research Services, National Institutes of Health, Bethesda, Md., recently delivered the 102nd Cutter lecture on preventive medicine at the Harvard University School of Public Health. His subject was, "Some Problems Arising in Prospective and Retrospective Studies of the Etiology of Disease."

LOUIS DUPREE, associate professor of anthropology at Pennsylvania State University and research associate in the department of anthropology at the American Museum of Natural History, New York, left in June to represent the American Universities Field Staff (New York) in Afghanistan and Iran.

FRANCIS W. HUNNEWELL, botanist and research associate in Harvard University's Gray Herbarium, will retire on 30 June. Botanical research was a second career for Hunnewell, who has been a Boston lawyer and an administrator at Harvard. He received his A.B. from Harvard College in 1902. While associated with the Gray Herbarium he made many collecting trips, mostly in the West Indies, the Canal Zone, and South America.

HANS WYNBERG, associate professor of chemistry at Tulane University College of Arts and Sciences, will study at the University of Leiden, Leiden, the Netherlands, during the academic year 1959–60.

LAURENCE L. QUILL, head of the chemistry department at Michigan State University, has been elected president of Associated Midwest Universities. He succeeds JAMES H. JENSEN, provost of Iowa State College. Other newly elected officers include: ROBERT S. SHANKLAND, professor of physics at Case Institute of Technology, Cleveland, Ohio, vice president; JOHN H. ROBERSON, executive director of AMU, secretary; ARTHUR T. SCHMEHLING, assistant business manager, Northwestern University, treasurer.

Book Reviews

Patterns of Discovery. An inquiry into the conceptual foundations of science. Norwood Russell Hanson. Cambridge University Press, New York, 1958. x + 241 pp. Illus. $5.50.

In my opinion, this is the most exciting book on the philosophy of science to appear in the last 10 years. It is exciting for various reasons, but the most important single reason is that at last we have a philosopher of science who is in fact writing about science and not about the papier-mâché constructions that frequently replace science in the writings of philosophers and logicians of science. Moreover, the realism (and thereby the novelty) of the approach strikes the reader from the early chapters of the book on. By the time one has reached the chapters on theories and on classical particle mechanics one has been introduced to what is almost literally a new way of *seeing* science—a way of seeing that enables one to remove the usual philosophical puzzles about "the reality of theoretical entities" and about "induction" from the all-too-central position that they normally occupy in the philosophy of science and to replace them with an undistorted view of a modern research science in full life.

Not only does Hanson know science but he has the requisite skills in logic and conceptual analysis for an undertaking of this scope. Thus, the need that his book fills is a complex one: the need for someone to write about science who has the technical equipment of a first-rate philosopher, the ability to see science as it is, and the good sense not to force it into one or another tidy schematism.

In order to explain Hanson's achievement it is necessary to describe briefly the conventional account of science. According to this account, observation reports in science are couched in one vocabulary ("the observation vocabulary") and theories are couched in another ("the theoretical vocabulary"). The "observation vocabulary" is thought of as stable and unchanging (in contrast to the highly changeable "theoretical vocabulary"). Observational reports are admitted to be corrigible, but the emphasis, by and large, is on the procedures by means of which theories are checked or tested against observation reports (which, it is assumed, any careful observer can verify with only a very small probability of error). Theories are entertained by scientists for various reasons, but the question of why a scientist entertains a theory (as opposed to how he tests it, once it is formulated) is dismissed as a question for "psychology" rather than logic. (Hanson points out in passing that this approach dismisses precisely the job that requires the genius—the Einstein, the Newton, the Kepler—from study by philosophers of science and focuses on the job that any well-trained graduate student can do.) The testing of theories is, in turn, treated as a basically simple matter; predictions (couched in the "observation vocabulary") are derived, and, if they turn out to be true, the theory is accepted. Insofar as considerations other than predictive success enter into the acceptance and rejection of theories, these considerations are usually lumped together under the name "simplicity" (some speak even more vaguely of the scientist's search for the "simplicity" of his "total conceptual system").

Now, this conventional philosophy of science has been running into increasing difficulty in late years. Hempel, for example, has pointed out a number of very serious difficulties in the attempt to make the notions of "testability" and "simplicity" precise, while Quine (following the lead of the 19th-century Duhem) has urged that the whole idea that scientific laws must be testable in isolation is a serious mistake. But these contributions are in technical articles that are unlikely to be encountered by the scientist or the scientifically trained layman interested in the conceptual foundations of science. Here, however, is a book-length treatment which, in addition, does more than criticize the "hypothetico-deductive" account at isolated points; it replaces it boldly and from the outset, not just with a different account but with a different (and more suggestive) set of questions.

Hanson begins by challenging the separation between "observation" and "inference" which contemporary philosophy of science has inherited from the positivism of the 1930's. Amplifying some remarks of Wittgenstein's on *seeing*, he stresses the extent to which even ordinary "garden variety" cases of "seeing" an event involve integration and organization, and he establishes the essential falsity of any account which separates this into two temporally or even logically distinct stages: first seeing the bare "sense datum" and then drawing "inferences." Scientists with different conceptual schemes, he argues, do not simply draw different inferences from a common stock of observation reports; they *observe* different things.

After this preliminary reexamination of the concept of *seeing* (and, by implication, of observation), Hanson moves to his central topic: the processes by which theories are arrived at, as opposed to those by means of which they are checked. Replying to the contention that this must be left for "psychology," he rejoins: "In the thinking which leads to general hypotheses, there are characteristics constant through the history of physics, from Democritus and Heraclitus to Dirac and Heisenberg" (page 72).

Hanson's discussion of the "patterns of discovery" is complex, and I shall only give hints of what it contains. Among other points, it stresses the role of unwieldy notations in hindering the discovery of a successful way of organizing data, and the somewhat surprising fact (illustrated by several novel examples from the history of science) that even after the "right" notation has been arrived at, there may still be trouble because the right notation "comes" initially with the wrong physical interpretation. (Kepler was already working with elliptical orbits as a mathematical device while he still subscribed to the theory that the orbit of Mars is an ovoid.) Hanson's account also includes a fresh discussion of the concept of causal explanation and of the role played in causal explanation by "theory-loaded" words. One point of which I heartily approve is this: he stresses the role of theories throughout, not just in prediction but in making nature intelligible. Once one has seen how theories are built into the concepts we use, and how a successful theory comes to be presupposed in a host of predictive, explanatory, descriptive, and computational contexts, one can also see why it is that a scientist will instantly reject one theory that "flashes into his mind" while deciding to pay serious attention to another—although both agree with the data from which he is working and neither has otherwise been tested.

A number of important points in the logic of science follow from this account. One of the most important is this:

since a theory may be built into the concepts we use in the description (in fact, in the very observation) of phenomena, to give up an important scientific law would be to do more than to give up some predictions we had become fond of making; it would be to "let our concepts crumble." Thus it can be that the abandonment of a scientific law may be a *conceptual* impossibility notwithstanding the fact that the law is empirical in the sense of aiding in the derivation of testable predictions. To put it differently, certain scientific laws (for details, see Hanson's chapter on classical particle mechanics) are *not* "empirical" in the sense that no experiment now conceivable (and this is not a "psychological" use of *conceivable*!) could overthrow them, although they are not "definitions," and they are not "a priori" either (since their abandonment *would* be conceivable if an Einstein or a Newton were suddenly to provide us with a whole new way of conceptualizing the phenomena in question). Since I feel strongly that overworking of the "empirical statement-or-else-a-definition" dichotomy is one of the worst faults of conventional philosophy of science, I was extremely happy to see Hanson take this up so thoroughly and so convincingly. Indeed, Hanson shows in detail how the same law may function in one context as a testable generalization, in another as a definition, in another as a conceptually a priori statement, and in yet another as a computing device. (I would only add: one should stress the point that the law does not have different *meanings* because it is employed in so many ways; sentences in a natural language—and not just laws—can quite frequently be used in so many different ways *because* they have a single meaning.)

Among other problems touched on in these chapters are the familiar worries about the "reality of theoretical entities" (what better reason could there be for accepting a system of concepts than that it makes the world intelligible?) and the difficulties that some have felt about the use of exact numbers in theoretical science. The book culminates in a chapter on elementary particle mechanics which shows the power and fertility of Hanson's ideas through their ability to render some of the dark mysteries of quantum mechanics understandable, not in the sense of providing final clarification (that is the goal of the physicist rather than of the philosopher of science) but understandable in the context of the past history of scientific theory-construction, and in the context of a growing research science.

HILARY PUTNAM
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Princeton University

Plain Talk from a Campus. John A. Perkins. University of Delaware Press, Newark, 1959 (order from University Publishers, New York). x + 195 pp. $4.

Since their average tenure is less than 5 years, many state university presidents are not in office long enough to reflect very much upon their experiences, much less reduce them to book form. John A. Perkins, president of the University of Delaware since 1950, is one of the exceptions. He speaks not only as an experienced educational administrator but also as one who has achieved recognition in the field of public administration. His *Plain Talk from a Campus* is a sharp analysis and a searching commentary on some of the critical problems in contemporary American education.

Part 1 deals with the purposes of education, both higher and secondary. According to the author, colleges and universities confront four main sources of problems: overwhelming increases in enrollment; the extremely divergent preparation of high-school graduates; the tendency of most institutions to "emphasize tradition far more than change"; and the peripheral functions which barnacle the pilings of American education. In view of the fact that higher education enrollments quintupled during the first quarter of the present century and doubled in each subsequent 15-year period, one may wonder how "overwhelming" our problem of sheer numbers is, but there can be no question about the fact that Perkins has come to grips with some of the major educational issues of our time.

In Part 2, his analysis of the problems of financing higher education, particularly on the state level, is very incisive. What he has to say about the shortcomings found almost everywhere in the patterns of state expenditure and taxation makes very understandable the fiscal fumblings of many state legislatures, and one must agree with him that more federal support is inevitable if these mounting difficulties are not overcome. In his opinion, moreover, bringing the Federal Government more largely into the picture implies no new peril.

Perkins' special interest in public administrations is reflected in the third part of the volume. He stresses the role that the colleges and universities ought to play in training students for public service careers, and he urges a wider realization of what Walter Lippmann has called "the public philosophy." A telling contrast of a wryly amusing sort is drawn between American political leadership of the past and present, in a chapter on "Benjamin Franklin and the organization man."

The final section of *Plain Talk from a Campus* is a potpourri, having to do with such miscellaneous topics as the ingredients of effective university administration, research and publishing, the neglected importance of books as media for learning, what a president does and does not include in his annual report, and the need among students for more self-discipline.

All in all, John A. Perkins has given us some plain talk which needs to be heard and heeded within and around all of our campuses.

LOGAN WILSON
University of Texas, Austin

Trend and Tradition in the Prehistory of the Eastern United States. Illinois State Museum Scientific Papers, vol. 10. American Anthropological Association Memoir No. 88. Joseph R. Caldwell. Illinois State Museum, Springfield, 1958. xiv + 88 pp. Illus.

This synthesis of the archeology of the eastern United States, originally written as a doctoral dissertation at the University of Chicago, should prove most valuable as a general introduction to the subject. It has the advantage over previous syntheses, such as *Archeology of Eastern United States,* edited by James B. Griffin (University of Chicago Press, 1952), of being a true synthesis and not just a compendium of local sequences. On the other hand, it avoids the disadvantage of *Method and Theory in American Archaeology,* by Gordon R. Willey and Philip Phillips (University of Chicago Press, 1958), in that the synthesis is expressed in narrative fashion and is not compressed into a rigid scheme of developmental stages based primarily upon what happened in nuclear America. The present volume is truer to events in the eastern United States.

The acknowledged weakness of this synthesis is that, for lack of time to cover the literature thoroughly, the author concentrated on the southeastern United States, where he has done most of his own research. On the other hand, the volume does present fresh material on Southeastern archeology, and, if any area is to be emphasized, this is the best, since the most important developments took place here, at least during the later periods. The volume also suffers from a certain vagueness of conceptualization—for example, *trend* and *tradition* are not precisely defined, and neither are most of the actual trends and traditions covered in the monograph.

The author sees three major trends in the prehistory of the eastern United

States. The first, culminating in late Archaic time at the beginning of the first millenium B.C., was marked by increasingly efficient adaptation to the forest conditions peculiar to the area. In the second, spanning the period from 1000 B.C. almost to A.D. 1000, "we find reared upon this economic foundation an era of regional differentiation and stylistic change." The third trend was towards closer relationships with Mesoamerica—"progressive drawing together with the Nuclear American civilization" (pages vii–viii). This seems a reasonable way to characterize what happened in the area.

IRVING ROUSE
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Yale University

Elementary Practical Organic Chemistry. Part 1, *Small Scale Preparations*; part 2, *Qualitative Organic Analysis*; part 3, *Quantitative Organic Analysis*. Arthur I. Vogel. Longmans, Green, New York, 1958. xxviii + 890 pp. Illus. $9.75.

This new edition of *Vogel* differs from the 1948 edition chiefly in three respects: (i) the material dealing with the reactions and characterization of organic compounds and the tables of physical constants of the various classes of compounds and of their derivatives have been removed from the portion of the text dealing with preparative methods and added to the section on qualitative organic analysis, which now occupies 296 pages; (ii) an entirely new section (196 pages) has been added, on the quantitative estimation of nitrogen, halogen, and sulfur, of the common functional groups, and of a few specific compounds; (iii) there is a marked decrease in the number of compounds for which preparative procedures are given.

In Part 1, "Small Scale Preparations," the number of preparations given (approximately 150) is about 35 percent of the number in the 1948 edition. This reduction results not only from the addition of the new section on quantitative analysis but also from the fact that there are now fewer pages in part 1 and that the page-size has been reduced, the amount of text being about 75 percent of that in the 1948 edition. However, 150 is still a much larger number of preparations than one finds in most texts published in the United States. Moreover, there is a broader coverage of the theory of physical methods and experimental techniques.

Numerous changes have been made in the procedures given for preparing certain compounds, and new types of reactions, such as reductions with lithium aluminum hydride and sodium borohydride, have been added. On the other hand, the elimination of such a large number of preparations has necessarily meant a loss of useful types, and not everyone will be satisfied with the choice of those retained.

The author emphasizes the change to smaller-sized runs; the amounts used appear to be from one-fourth to one-tenth of those used in procedures given in the 1948 edition. However, the quantities of starting materials, which vary from a few grams to 25 grams and usually amount to around 15 grams, are comparable to the quantities usually used in laboratory courses in the United States. More sizes and types of glassware are used in the procedures given than are usually supplied for average-sized classes in the United States.

The organization of part 2, on qualitative analysis, is not the best possible. The familiar system developed at the University of Illinois is used, but the two chapters titled "Reactions of organic compounds" and "Class reactions" cover much the same material. Similar or identical procedures may be found in the two chapters, some tests are given in one chapter and some in the other, and directions for preparing derivatives are found in both, along with qualitative tests for functional groups. The inclusion of separate discussions for aliphatic functional groups and aromatic functional groups leads to much duplication and to many unnecessary cross references.

Part 3 describes, for the most part, standard procedures for the determination of functional groups. In fact, all three parts (which, incidentally, may be purchased separately) are very similar to texts published in the United States that cover the same areas.

CARL R. NOLLER
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Stanford University

Dangerous Marine Animals. Bruce W. Halstead. Cornell Maritime Press, Cambridge, Md., 1959. vi + 146 pp. Illus. $4.

Although this volume contains a remarkable amount of information about the kinds of marine animals that are dangerous to man (dangerous when touched or eaten or when overtly aggressive), we are assured that this book is the nonspecialist's version of a more exhaustive book still in preparation.

With the growing use of diving equipment, doctors especially will find this a valuable reference book, for the author (a physician) has taken pains to discuss the medical aspects of all sorts of marine accidents, ranging from jellyfish stings and poisoning from shellfish to sea-snake bites. An amazing variety of animals are in some way dangerous to man, but so little is known of many of them, or even of the nature of the injuries they cause, that many of the recommended treatments are empirical guesses. If one is bitten by a sea snake, it is essential that the snake be brought along to the hospital to make sure it is harmless. Much evidently remains to be learned, especially about the nature of fishes that are poisonous to eat, before the resources of the "silent world" can fulfill the expectations of some hopeful people. In the meantime, a book such as this is an essential beginning.

JOEL W. HEDGPETH
Pacific Marine Station,
Dillon Beach, California

The Perpetual Forest. W. B. Collins. Lippincott, Philadelphia, 1959. $4.50.

W. B. Collins, who is deputy chief conservator of forests in Ghana, has managed to capture on paper much of the drama of life, death, and renewal in the African tropical forest. Any naturalist who has spent years of his life in the equatorial forest has felt the silent force, the rich complexity and ecological integration, of this most interesting of our terrestrial communities. Without saying so, Collins conveys by an array of facts the impression that the forest itself is a living, pulsating organism.

The author describes the conditions for the existence of a rain forest; he starts with the organisms in the soil, then discusses the succession from the relatively simple pioneer stage of the mangrove swamp to the complex, varied, climax forest. Today this self-sufficient world is being assaulted by man, and the destruction of the closed forest may be accomplished within the century. Collins describes the step-by-step process by which this occurs—the destruction of the forest cover and, finally, of the land, much as it occurred in North America. But water and wind act with cataclysmic force in the tropics.

The original shifting cultivation of the native garden was not destructive because these cultivated areas, abandoned after two years, were regenerated in another ten. But, as population increases, the rest periods become too short and new forest openings are burned out constantly. Once cleared of forest, the ground, laid bare to the searing sun, ceases to function as it did before it was denuded. First, the breakdown of humus is accelerated, then soil organisms are killed. Wind erosion follows. Rains may come, but there is no organic material

left for the soil microorganisms to work on. Destruction of the key organisms in the food chain destroys the community. Gulley erosion on denuded land, when the rains come, completes the destruction. There is some reforestation, but this occurs at the expense of the closed forest, which includes too many species of no commercial value.

The first few chapters of *The Perpetual Forest* are strongly ecological in approach; the latter half of the book becomes almost anecdotal as group after group of animals is discussed to illuminate some part of the total picture. There is an interesting chapter on termites, driver ants, and other insects. There is a chapter on snakes and one on birds, and Collins understands and describes the dependence of animals on food niches.

He has a flair for vivid expression, but this is sometimes rendered less effective than it might have been through injudicious use of the comma. It was to have been expected that Collins, in studying the whole forest, would wander into fields in which he is not expert. His estimate of the age of the tropical forest as only a million years, when there is fossil evidence that it is 100 million years old, suggests a "blind spot." But these details do not seriously detract from the value of this book as a picture of the West African rain forest.

W. J. BEECHER
Chicago Academy of Sciences

Programming for an Automatic Digital Calculator. K. H. V. Booth. Academic Press, New York; Butterworths, London, 1958. 238 pp. $7.50.

It is a good thing that this title reads *"Programming for an Automatic Digital Calculator"* rather than "Programming for Digital Calculators," for the reader will find the discussion limited to the APEXC, a computer at Birkbeck College, London.

The mathematical level of the exposition is fairly elementary. One can believe the author's statement, "the technique for programming can be acquired by anyone with a capacity for accurate detailed thinking, and a talent for solving puzzles. Moreover, it has been our experience that it is possible to train people to do useful programming in a matter of two weeks, although the acquiring of the more subtle tricks of the trade naturally takes longer." One can also say that the book will be invaluable to anyone faced with the problem of programming an APEXC computer. The relevant functional organization of the machine, detailed descriptions of various routines (such as division, square root, matrix operations, and the solving of simultaneous linear equations), and fault-finding are discussed at length. Glimpses are also provided of more exotic topics, such as mechanical translation and automatic programming.

The book is not likely to have wide appeal for computer programmers or engineers for the following reasons: general problems of logical programming are not discussed; only the more elementary routines are considered; and much of the detailed discussion bears only on the Birkbeck machine. An experienced programmer, who can translate the discussion into a form applicable to his own machine, may find useful hints and kinks.

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Reports

Low-Level Irradiation and Threshold Shift in the Visual Receptor

Abstract. Customary methods of stimulating and recording were used to examine threshold shifts of the single visual receptor in the lateral eye of *Limulus* in response to low-level x-irradiation. Marked visual sensitization was found and was most pronounced at the lowest dosage levels (1 to 25 r). Complete light adaptation apparently cancelled the effects of the irradiation.

Since World War II, a large number of investigations of the effects or ionizing irradiations on various kinds of behavior have been carried out. The behavior associated with the visual mechanism, however, has not been investigated to any great extent and generally has been studied with respect to relatively high doses of irradiation.

Cibis *et al.* (*1*) concluded that irradiations of 1700 r will destroy the rod cells of some mammals and that doses upward of 10,000 r will cause the destruction of the cone cells. Kektcheew (*2*) reported that doses of lower intensity produce a drop of visual sensitivity which maintains itself for several days. Lenior (*3*) used the Birch-Hirschfeld adaptometer to investigate the course of dark adaptation before and after x-ray treatment. He noted a decrease in facility of adaptation after the administration of the x-rays. Furchtgott (*4*) found that a total body dose of 369 r of x-irradiation caused a decrement in a brightness discrimination by rats.

The purpose of the present program of research (*5*) is to study further the effects of x-irradiation on the visual mechanism by using the *Limulus polyphemus* (L) or "horseshoe crab," an animal whose visual functions have been thoroughly studied (*6*). The experiment reported here was designed to examine the cumulative effects of low doses of x-irradiation on the dark-adapted threshold of the eye of *Limulus*.

Nineteen single optic nerve fiber preparations were made from the lateral eye of *Limulus*. Sixteen of these were used for the collection of experimental data, and three were used for control. The methodology utilized in securing the single unit, or single functional unit, was similar to that of Hartline (*6*), with the following exceptions: The constant-temperature solution used to bathe the excised eye was fresh sea water held at 15° ± 0.1°C, to which 4 percent reagent quality ethyl alcohol had been added. This addition was made as a precaution against possible lateral inhibition (*7*).

Once a single unit had been secured, a plastic top, whose interior contained a flat sponge saturated with sea water, was placed over the preparation to maintain a high moisture level. At this point a stimulus spot 1 mm in diameter was used to locate the corresponding ommatidium, and the preparation was allowed to dark-adapt for 30 minutes.

At the end of the dark-adaptation period, the threshold of response to a 1-second presentation of the stimulus spot from a ribbon-filament, 6-volt incandescent bulb was determined by the ascending series of the method of limits (*8*). The intensity of the stimulus spot was controlled by a circular, neutral-density optical wedge previously calibrated in tenths of a log unit. Threshold checks were accomplished at 10-minute intervals, and the response to each presentation of the stimulus was recorded photographically. The results of the analysis of the control data are shown in Fig. 1 (top) and are similar to those found by Hartline (*9*).

The thresholds of the 16 experimental preparations were recorded in like manner. Immediately following dark-adaptation, three consecutive threshold determinations were made; these are shown to the left of time zero in Fig. 1 (top). On completion of these determinations, five irradiations (*10*) of 5 r each were delivered. The threshold was redetermined after each irradiation. Further irradiation was delivered in increments of 25 r, each increment being followed by a measurement of the threshold. The mean results of these determinations are shown in Fig. 1 (top), in which the time scales for the experimental preparations and for the controls are comparable.

Five of the 16 experimental preparations were adapted to light at room intensity for 15 minutes at the end of the 200-r dose and then dark-adapted once more. The recorded threshold to this adaptation level is shown in Fig. 1 (bottom).

Apparent sensitization of some portion of the visual mechanism occurs as the dosage of irradiation accumulates. The course of sensitization is negatively accelerated. Probably of greatest interest is the pronounced shift of threshold at low dose levels. The locus of this effect may be in any or all of three systems: the photochemical system of the retinula cells, the eccentric cell, or, possibly, the axon itself.

It seems unlikely that there is an effect in the chemical systems which mediate the propagated potential. There is evidence to support the view that nervous tissue is insensitive to less than lethal dosages (*11*). It seemed possible to localize the effect to the photochemical system of the retinular cells by the light-adaptation–dark-adaptation procedure. Preliminary experiments had established

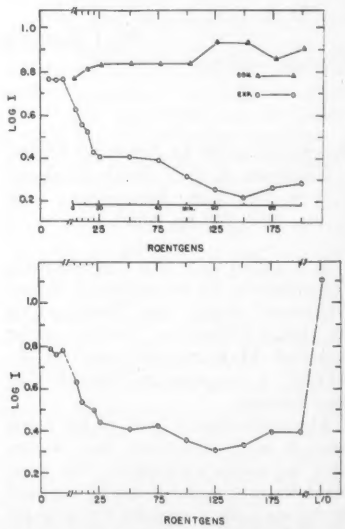

Fig. 1 (Top) Visual dark-adapted threshold measures for single-unit preparations from the lateral eye of *Limulus*. The thresholds of the experimental preparations were measured during cumulative x-irradiation; thresholds for nonirradiated controls were determined at comparable time intervals. (Bottom) Thresholds for dark-adapted preparations similar to those represented in Fig. 1 (top), as a function of cumulative irradiation. After x-irradiation of 200 r, the preparation was light-adapted and then dark-adapted, and the threshold was again determined.

Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should *not* repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper.

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to *one* 2-column figure (that is, a figure whose width equals two columns of text) or to *one* 2-column table or to *two* 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [*Science* 125, 16 (1957)].

that the shift in threshold of response to irradiation was of a stable nature under dark-adapted conditions and remained constant after the final irradiation at 200 r. The threshold was determined at irregular intervals on some preparations for as many as 6 hours with no apparent return to normalcy.

Light-adaptation apparently serves to cancel the effects of irradiation on the system when the receptor is once more dark-adapted and the threshold is again measured (Fig. 1, bottom). The disparity between this sensitivity level and the terminal sensitivity of the controls is no more than might be attributed to pathological decay of the system. A similar control point may be extrapolated from the data by extension of the curve for an equivalent length of time. On this basis we may tentatively place the locus of effect in the photochemical system.

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24 March 1959

Paper Coal in Indiana

Abstract. The foliated, papery texture of the upper third of an 18-inch coal seam in a strip mine near Rockville, Indiana, is attributable to matted plant cuticle. The cuticles of pinnules, pinnae, and rachides resemble *Sphenopteris bradfordii* Arnold and thus differ from the lycopsid stem cuticles of the Russian paper coal.

In 1860 Auerbach and Trautschold (*1*) reported the occurrence of an unusual type of coal in the Moscow Basin of central Russia. This unique *Papierkohle,* as they called it, has been the subject of several reports and numerous discussions by geologists and botanists since then. The plant cuticles which make up the Russian paper coal are the remains of twigs of arborescent lycopods, although their specific botanical affinity has been the subject of considerable controversy. Auerbach and Trautschold (*1*) named the cuticles *Lepidodendron tenerrimum.* Walton (*2*) assigned them to the genus *Bothrodendron,* Bode (*3*) to *Porodendron,* a genus belonging to the eligulate Lycopodiales. Bode distinguished two species, *Porodendron lepidodendroides* and *P. pinakodendroides.* Figure 1, *A* and *B,* shows cuticles that occur in the Russian *Papierkohle.*

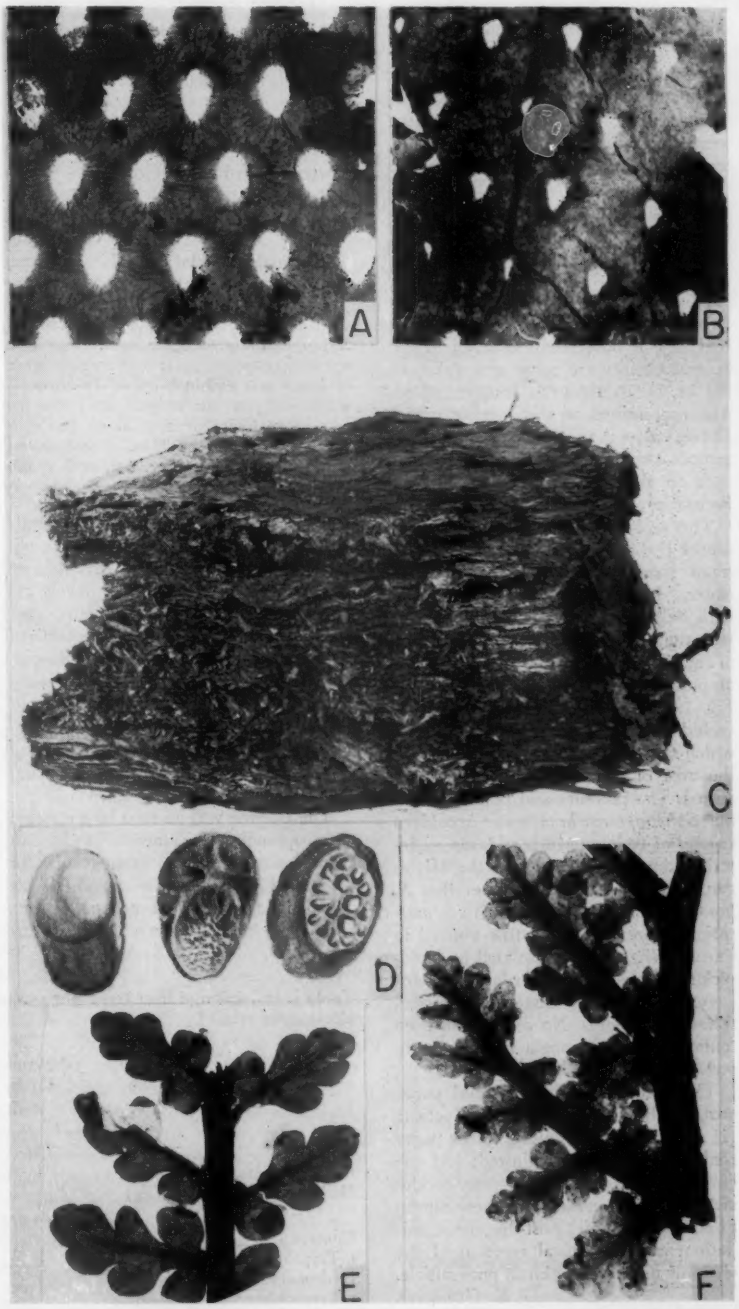

Fig. 1. *A, B,* Cuticle from the Russian paper coal (*7*) (about × 2). *C,* Block of Indiana paper coal (about × ¼). *D,* Drawings of Torispora specimens (about × 250). *E, F,* Parts of pinnae from Indiana paper coal (about × 2).

In January 1958 one of us (R.C.N.) discovered a paper coal in the high wall of a strip mine about ¾ mi north of Nyesville, near Rockville, Parke County, Indiana (SW¼SW¼ sec. 27, T.16N., R.7.W., Rockville Quadrangle). The upper 6 inches of the 18-inch coal bed is brown and leafy, like the yellowed pages of a book (Fig. 1, *C*). The lower 12 inches of the coal is solid, not papery. The paper coal layer is composed of matted plant cuticles and abundant spore exines embedded in vitrinitic attritus. Opaque attritus and anthraxylon are extremely sparse. The flexible aspect is most evident at the outcrop, where weathering has removed much of the interstitial vitrinite. An unusual sporelike body, named *Torispora* by Balme (*4*) and called *Bicoloria* by Horst (*5*), has been observed in abundance in the Indiana paper coal (Fig. 1, *D*).

The exact stratigraphic position of the Indiana paper coal has not been determined. Spore analyses of the paper coal and of other coals exposed in the general vicinity are being undertaken to aid in the stratigraphic interpretations. The coal mined at this locality, about 12 feet below the paper coal, has yielded a spore assemblage which indicates that it is in the Brazil formation (Upper Pottsville).

The cuticles which give the papery aspect to the coal are remains of small stems and leaves. Agitation in water, hand-picking, and treatment with Schultze's reagent and 12 percent potassium hydroxide facilitate separation of individual membranes of cuticle. Examples of isolated cuticles are shown in Fig. 1, *E* and *F*. Pinnules, pinnae, and rachides of ancient fernlike foliage, which must have grown in profusion in the area of coal deposition, are represented. The pinnules and pinnae resemble *Sphenopteris bradfordii* Arnold, a species of lyginopterid pteridosperm described by Arnold (*6*) from the Michigan Coal Basin. Arnold states that *S. bradfordii* may be identical with *S. marrati* Kidston. Sporangia, first noticed in thin sections and later isolated by hand-picking, consist of an outer layer of *Torispora* and a central mass of compressed, thin-coated spores. No seeds have been found, and no sporangia have been observed attached to cuticles.

The occurrence of this unusual paper coal can be attributed to three factors: (i) the foliage contributing to the paper coal was thoroughly cutinized; (ii) the environmental conditions were conducive to the preservation of these masses of cuticle; and (iii) post-diagenetic oxidation and mechanical removal of the vitrinitic attritus left almost pure cuticle.

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22 October 1958

Pattern of Adaptive Control of Levels of Rat Liver Tryptophan Transaminase

Abstract. The dual control by substrate and hormone of the level of a third adaptive enzyme in animals is described. Injections of hydrocortisone or the substrate tryptophan increased the level of the liver tryptophan-α-ketoglutarate transaminase of intact rats within 5 hours. In adrenalectomized rats this enzyme level was increased by hydrocortisone alone, but substrate induction could be demonstrated only if these animals were treated at the same time with hydrocortisone.

The level of tryptophan-α-ketoglutarate transaminase in liver is approximately doubled after hydrocortisone treatment of rats (*1*). The levels reported here, determined 5 hours after treatment of intact or adrenalectomized albino rats of either sex with hydrocortisone or with the substrate tryptophan, showed that this is a new example of substrate and hormonal induction (adaptation) of an enzyme in animals, and one whose pattern of control is like that of tyrosine transaminase (*2*).

The enzyme was assayed by a specific spectrophotometric method (*3*) in freshly prepared liver homogenates of individual animals. The mean levels found in the different groups of rats (Table 1) indicate that a significant increase in tryptophan transaminase activity occurs in the intact rat after treatment with tryptophan and that a greater increase occurs after treatment with hydrocortisone.

In order to determine whether induction of the enzyme by the substrate can take place in the absence of adrenal cortical activity, adrenalectomized rats were studied 4 days after operation. After removal of the adrenals, the basal level of tryptophan transaminase fell somewhat below its level in intact animals. Injection of tryptophan produced a small rise in enzyme activity which was not statistically significant. The same or no response was produced by injections of D-tryptophan and the four analogs of tryptophan, α-methyl-DL-tryptophan, 5-methyl-DL-tryptophan, 6-methyl-DL-tryptophan, and DL-tryptazan. However, hydrocortisone treatment of the adrenalectomized rats still produced a significant (62 percent) increase in activity above the basal level. When L-tryptophan and hydrocortisone were given simultaneously to the adrenalectomized rats, the activity increased 167 percent above that of the adrenalectomized controls.

These results indicated that hydrocortisone is a stimulus sufficient to increase the enzyme activity in both the intact and adrenalectomized animals. On the other hand, the response to tryptophan found in intact animals was almost completely abolished by adrenalectomy. The potentiating effect of tryptophan on the enzyme level in the hydrocortisone treated, adrenalectomized animals indicated that there is a specific substrate-inducing effect, but only in the presence of adrenal cortical hormones. This occurred when the hormone was either released by the stress of substrate injection in the intact animals or when it was administered to the adrenalectomized animals.

The adaptive increase of this enzyme which is produced by corticoid stimulation alone, but by the substrate only in corticoid-treated animals, is identical

Table 1. Induction of liver tryptophan-α-ketoglutarate transaminase of intact and adrenalectomized rats.

Treatment	No. of animals	Mean activity of enzyme*	Change from controls	
			Percentage	*P*
Intact rats				
Control	8	14.2 ± 4.38		
L-Tryptophan (0.5 g/kg)	4	21.0 ± 5.2	+ 50	< .02
Hydrocortisone (30 mg/kg)	6	37.0 ± 7.46	+ 161	< .01
Adrenalectomized rats				
Control	4	10.6 ± 2.6		
L-Tryptophan (0.5 g/kg)	4	12.3 ± 2.8	+ 16	0.40
Hydrocortisone (15 mg/kg)	4	17.2 ± 1.8	+ 62	< .01
L-Tryptophan (0.5 g/kg) plus hydrocortisone (15 mg/kg)	4	28.3 ± 6.2	+ 167	< .01

* Activity is expressed as micromoles of indolylpyruvate formed per hour per gram of dry liver plus or minus standard deviation.

with the pattern of control established for the somewhat larger adaptive changes of the tyrosine-α-ketoglutarate transaminase (*2*). A corticoid-induced "metabolic state" (*4*), perhaps the basis for the "permissive" action of cortisone, is considered to be required for these two adaptive responses to the substrate stimuli. In contrast, the tryptophan pyrrolase (peroxidase-oxidase) level is also increased by corticoids, but the substrate is a sufficient stimulus by itself to adaptively increase this enzyme level (*5, 6*).

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29 January 1959

Growth of Body Weight and Manipulation of Food Motivation

Abstract. Consideration was given to the possible use of individual growth curves to estimate *ad libitum*–feeding weights as part of technique for producing specified degrees of food deprivation. In heterozygous animals, this possibility was found to be feasible but limited by the occurrence of discontinuous growth functions.

In experiments said to deal with "motivation" for food or requiring "hungry" animals as part of the procedure—for example, to maintain operant responding with food reinforcement—some type of operational specification of food deprivation must be selected. A common technique for manipulating this variable is rhythm feeding, where animals are allowed to eat *ad libitum* for a fixed time interval T every H hours. In Fig. 1 (top), sample data obtained from 12½-month-old, random-bred, male Wistar albino rats show some effects of this technique on body weight when the values of T and H are, respectively, 1 and 23 hours. The daily weight immediately before feeding is expressed as percentage of *ad lib.*–feeding weight, where this base value is the rat's average weight for the 10 days of continuous feeding immediately preceding the start of the rhythm schedule (*1*).

Body weights decrease over successive days of the procedure, and the extent of the decline differs among individual rats (*2*). This suggests that, if one wishes to produce a constant degree of deprivation from rat to rat, a better technique may be deliberate reduction of body weight to a specified percentage of the *ad lib.*–feeding weight. However, *ad lib.*–feeding weight changes with age, and it is frequently necessary to initiate relatively prolonged studies with rats that are still growing. Therefore, in attempting to hold such a percentage fairly constant with the passage of time, one might wish to recompute this weight at regular intervals, using the changing base weights. But once a deprivation procedure is launched, how are we to know the weights that would have prevailed with increases in age, had the animal been permitted to feed freely?

It seemed to us that one answer lay in the *ad lib.*–feeding weights to be *expected* in an animal at various ages. These might be determined by extrapolation from an appropriate equation fitted to some of the animal's prior age-weight data. To examine the feasibility of this notion, we maintained daily age-weight records for rats (all males) feeding *ad libitum* in our colony areas, and for each animal, individual weekly mean weights were computed for successive weeks of age. Plots of typical individual growth data, treated in this manner, are presented for heterozygous males of the Charles River CD strain (*3*).

The lower plot of Fig. 1 shows that satisfactory prediction of *ad lib.*–feeding weight is possible. The smooth curve drawn through the data points is for the equation

$$y = -9.82 + 34.77x - 0.56x^2$$

fitted by the method of averages to the initial data, which are shown as filled circles. Weight values obtained later, shown as open circles, are in fair agreement with the extrapolated portion of the curve. The other curve, labeled *D*, is drawn through the average weekly weights at which this rat might have been maintained in order to keep it at 80 percent of his predicted *ad lib.*–feeding weight.

Continuous functions prevailing over the age range reported here were found to be rare. The bulk of the individual growth curves we obtained appear to be discontinuous functions of the type seen in Fig. 2. The first segment is negatively accelerated. It may be a parabola, as in Fig. 1, but it may be a function of other forms, such as

$$y = c - ae^{-bx}$$

and (*4*)

$$\log y = a - b(1/x)$$

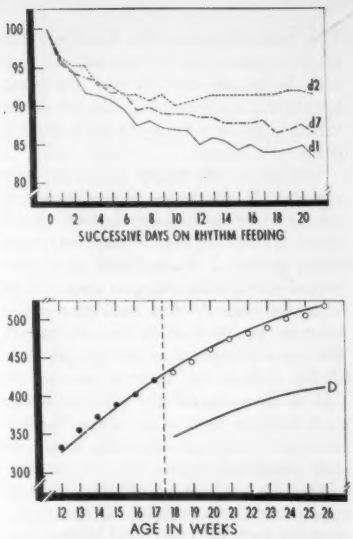

Fig. 1. (Top) Percentage *ad libitum*–feeding weight before eating as a function of successive days on a 23-hour feeding rhythm. Data from male Wistar rats. (Bottom) Individual weekly mean body weight in grams as a function of age in weeks for a male CD rat.

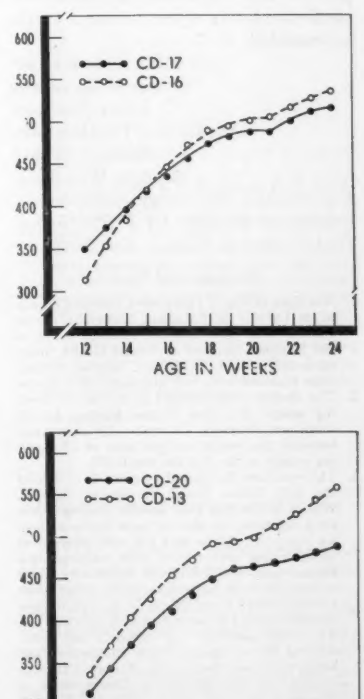

Fig. 2. Individual weekly mean body weight in grams as a function of age in weeks. Data from male CD rats.

The segment beyond the break may be similar, positively accelerated, or possibly linear. In our CD rats, the break occurred as early as 18 weeks, but in the Wistar rats it was generally not seen before 24 weeks.

Similar breaks might occur at later ages in CD rats whose curves currently appear to be continuous. Indeed, in the curve plotted in Fig. 1 (bottom), one might predict a discontinuity or a prolonged plateau beginning at about 31 or 32 weeks, since the first derivative of the function equals zero in that region. If this logic is applied to the sample data of Fig. 2, however, only in the case of CD-16 does occurrence of the break tend to agree with expectation. For the most part, discontinuities appear sooner than predicted (*5*).

The earliest age at which a discontinuity can be expected in heterozygous animals, such as the CD and Wistar rats, would appear, at present, to set the upper limit of the age range over which an extrapolation technique of this type could be usefully employed. If inbreeding were to yield more uniform individual growth curves, or if, through other means, the discontinuities could be eliminated or better understood, it is possible that the useful age range and predictive power of the technique might be extended.

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References and Notes

1. The data of Fig. 1 (top) were recorded by one of us (M.K.) at Columbia University during his tenure as post-doctorate research fellow of the National Institute of Mental Health under sponsorship of F. S. Keller. Similar findings were obtained with four additional Wistar rats.
2. The decline is not related to the *ad lib.*–feeding weight preceding rhythm feeding. In the seven rats observed, the rank-order correlation between this weight and per cent *ad lib.*–feeding weight on the 21st day was 0.179.
3. This work was facilitated by grant B-1273 from the U.S. Public Health Service to John R. Whittier. The CD rats, specific pathogen-free until shipment, are derived from Sprague-Dawley stock. All Wistar and CD rats referred to in this paper were treated alike, weighed on a dietary scale, and fed Purina Laboratory Chow in meal form. In our colony areas, temperature usually ranged from 75° to 78°F, and relative humidity varied between 40 and 50 percent.
4. The latter possibility was called to our attention by C. A. Slanetz while this report was being prepared. See L. M. Zucker, "Growth criteria," in *Rat Quality: A Consideration of Heredity, Diet and Disease* (National Vitamin Foundation, Inc., New York, 1953), pp. 3–22.
5. When parabolas are fitted to the data of CD-16 and 17 for weeks 12 through 20, and CD-13 and 20 for weeks 12 through 18, $dy/dx = 0$ for the respective ages of 20.8, 24.5, 25.8, and 22.8 weeks. Discontinuities seen in Fig. 2 appear at the respective ages of 21, 21, 18, and 19 weeks.

28 November 1958

Autoradiographic Study of Uptake of Tritiated Glycine, Thymidine, and Uridine by Fruit Fly Ovaries

Abstract. Synthesis of DNA occurs in the nurse cell nuclei of *Drosophila melanogaster* in an asynchronous manner, whereas synthesis of RNA occurs in all these nuclei simultaneously. Synthesized RNA is concentrated in the plasmosomes; subsequently nuclear RNA enters the cytoplasm of the nurse cell and eventually the oöplasm. Protein synthesis occurs in the nucleoplasm and cytoplasm of all the cells in the egg chamber.

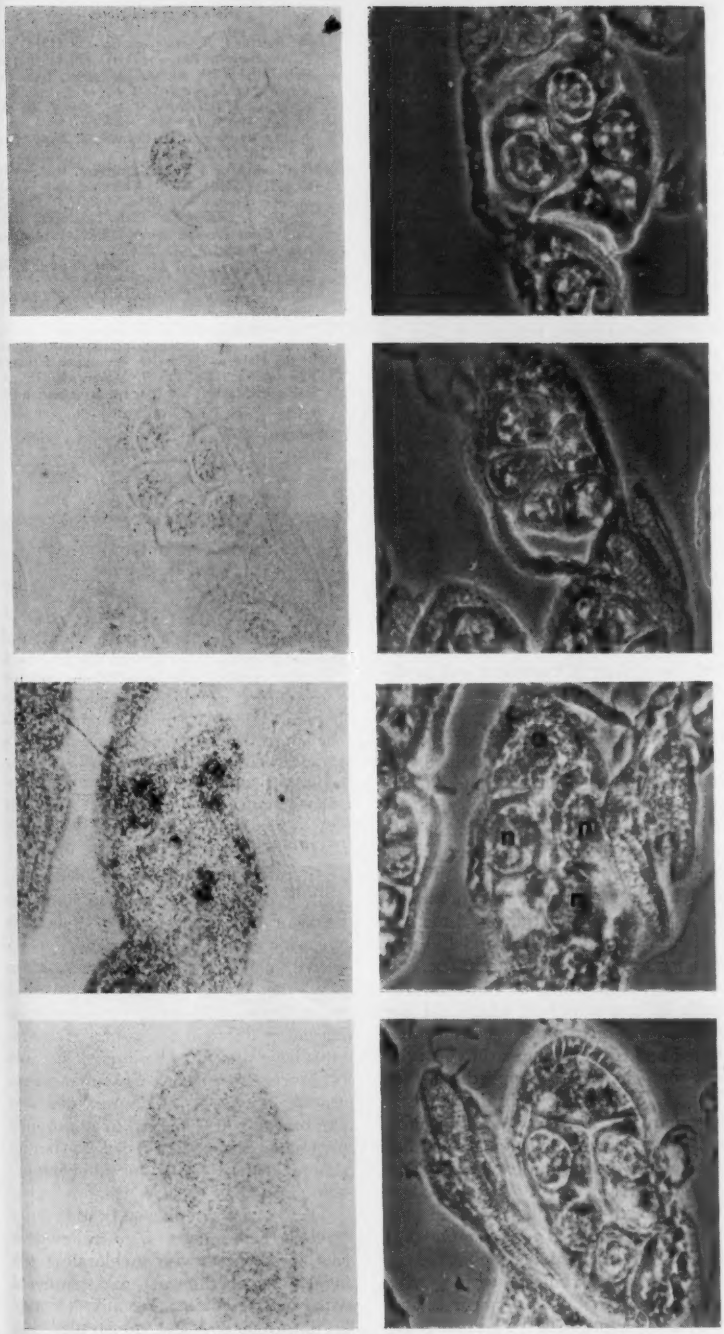
Six-hour-old, Oregon-R, wild type, adult, female *Drosophila melanogaster* were starved for 24 hours and then allowed to feed for 1 hour on a gram of yeast paste (two parts autoclaved, dry baker's yeast/three parts sterile water) containing either 25 μc of uridine-H^3 (1/40), 25 μc of thymidine-H^3 (1/87), or 250 μc of glycine-$2H^3$ (1/3720). The numbers in parenthesis refer to the ratios between radioactive and nonradioactive molecules in the respective radioactive solutions before the addition of yeast. The tritium atom of thymidine or uridine is attached to a carbon of the pyrimidine ring; the tritium atoms of glycine are attached to the amino carbon atom. Subsequently the flies were etherized (for the first time) and placed under insect Ringer's solution, and their ovaries were removed. The ovaries were fixed for 20 minutes in Kahle's fluid, dehydrated, infiltrated first with celloidin and then with paraffin and sectioned at 6 to 8 μ. The sections were mounted on albuminized slides, the paraffin was dissolved away, the tissue was then covered with stripping film (Kodak autoradiographic A.R.10), dried, and left exposed for 3 weeks at 3°C. The film was then developed and the preparation was coated with immersion oil (R.I.. 1.46) and viewed under bright-field and phase-contrast optics.

The silver grains observed occur above those molecules (presumably certain types of protein, RNA and DNA) made within the last hour of the fly's life which after Kahle fixation are insoluble in water, ethanol, benzene, methylbenzoate, and paraffin and which have glycine, uridine, or thymidine as precursors. Ovaries from flies fed glycine-$2H^3$ contained about 4 times, and ovaries from flies fed uridine-H^3 about 3 times, as much tritium as ovaries from flies fed thymidine-H^3 labeled, dead yeast.

The developing egg consists of a 16-cell nest surrounded by an envelope of follicle cells. The 16 cells are daughters which arise from four consecutive divisions of an oögonium. Fifteen of the daughter germ cells differentiate into nurse cells and nourish the most posterior, daughter germ cell which becomes the oöcyte. Intercommunication of cytoplasm between all members of the 16-cell cyst is made possible by pores in the walls separating adjacent cells (*1*). The development of the nest of 16 cells has been subdivided into a series of consecutive stages, ending with stage 14, the mature, ovarian, primary oöcyte (*2*). During the first seven stages all 16 germ cells grow at roughly identical rates. During stages 8 through 11 vitellogenesis occurs, and the oöcyte grows at a much faster rate than previously, at the expense of the nurse cells, which shrink and eventually degenerate. The follicular epithelium secretes first during stages 8 to 11 the vitelline membrane about the oöcyte and next during stages 11 through 13 the chorion. The ovaries observed contain oöcytes in stages 1 to 8 and 14 (plus an occasional one in stages 9 and 13). Stage 14 oöcytes (presumably formed prior to the first labeled meal) gave no autoradiograph.

It is known from the work of J. J. Freed [summarized by Schultz (*3*)] that nurse cell nuclei undergo a series of endomitotic doublings of DNA. In the case of the nurse cell nuclei observed in the thymidine study, the densities of the autoradiographs increased with increasing nuclear volume. However, not all the nuclei in an egg chamber showed an autoradiograph (Fig. 1), which indicates a nonsynchronous synthesis of DNA among the 15 nurse cell nuclei of an egg chamber. Tritium from thymidine was also localized in follicle cell nuclei.

On the other hand, tritium from labeled uridine was found in all the nurse cell nuclei in an egg chamber, which indicates that RNA synthesis is going on simultaneously in all the nurse cell nuclei of an egg chamber. Tritium from ingested uridine was distributed nonhomogeneously in nurse cell nuclei, and in large chambers (like those at stages 7 and 8) tritium can be shown to be localized mainly in the plasmosomes. The term *plasmosome* refers to an RNA-containing nucleolus. The tritium appeared first in the nurse cell nuclei (Fig. 2), and it subsequently appeared in the nurse cell cytoplasm as well, but at lower concentrations (Fig. 3). Similar densities of silver grains are found above the cytoplasm of nurse cells and the follicular epithelium. In stage-7 and -8 chambers the tritium in the follicular epithelium was concentrated to a greater extent in the nuclei than in the cytoplasm, but this nonhomogeneity in distribution cannot be demonstrated in earlier chambers because of the small size of the follicle cells. Under our conditions little tritium from uridine accumulated in yolky oöplasm and none in the oöcyte nucleus. In stage-13 oöcytes, tritium



Figs. 1–4. (Left, bright field; right, phase contrast; ×427). Fig. 1 (top). Stage-7 egg chamber from the ovary of a fly fed thymidine-H^3. The section passes through three nurse cell nuclei, only one of which gives an autoradiograph. Fig. 2 (upper middle). Stage-7 egg chamber from the ovary of a fly fed uridine-H^3. The section passes through five nurse cell nuclei, all of which give an autoradiograph. Fig. 3 (lower middle). Stage-8 egg chamber from the ovary of a fly fed uridine-H^3. The section passes through three nurse cell nuclei (*n*) and through yolky oöplasm (*o*). The density of developed grains is greatest above the nurse cell plasmosomes, next greatest above nurse cell nucleoplasm and cytoplasm and the cytoplasm of the columnar follicle cells (*f*), and least above the oöplasm. Fig. 4 (bottom). Stage-8 egg chamber from the ovary of a fly fed glycine-$2H^3$. Tritium is distributed homogeneously throughout the chamber.

from ingested, labeled uridine was localized in the epithelium surrounding the developing chorionic appendages.

In the case of ovaries labeled with tritium from ingested glycine, a homogeneous distribution of silver grains is seen above the chambers in stages 1 to 8 (Fig. 4). The concentration of grains rises with increasing chamber size. For example, autoradiographs above stage-8 chambers had 5 times as many grains per unit area as did those above stage-2 chambers. Since the stage-8 chamber has a volume 100 times that of a stage-2 chamber, the tritium content must be 500 times greater. In a late stage-9 chamber yolky oöplasm has about one-half as much tritium as the cytoplasm of nurse and follicle cells. Nurse-cell plasmosomes showed more tritium than the surrounding nucleoplasm. Stage-9 oöplasm may contain less tritium from ingested glycine than the cytoplasm of adjacent follicle cells because of the barrier provided by the newly synthesized vitelline membrane. Glycine can now enter the oöcyte only by way of the nurse cell chamber. Stage-13 oöcytes show an autoradiograph above the degenerating nurse cell nuclei and above the epithelium surrounding the developing chorionic appendages (*4*).

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References and Notes

1. See R. C. King and R. L. Devine, *Growth* 22, 299 (1958).
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4. This work was supported by the U.S. Atomic Energy Commission (contract No. AT(11-1)-89, project 12), the National Science Foundation (research grant NSF-G 4816) and by the graduate school of Northwestern University. Valuable technical assistance was performed by H. Pakeltis and A. Bartha. The labeled uridine and glycine were supplied by the New England Nuclear Corp. The labeled thymidine was supplied by Schwarz Laboratories.

23 January 1959

An Auxin-like Action of Coumarin

Abstract. Coumarin, usually regarded as an inhibitor of growth processes in plants, markedly stimulated the elongation of excised segments of *Helianthus* hypocotyls. Substitution in the molecule of hydroxy-, methyl-, or chloro-groups, in the neighborhood of the unsaturated bond in the lactone ring, markedly altered the growth-promoting activity.

Coumarin has long been known to be an inhibitor of germination and root growth (*1–3*). It has also been reported that coumarin inhibits auxin-induced elongation, as measured by the *Avena*

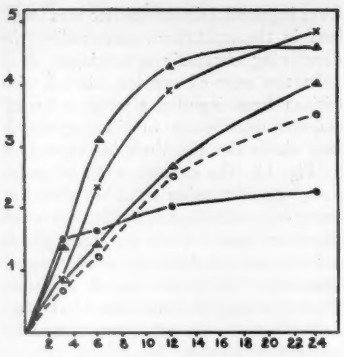

Fig. 1. The effect of coumarin in various concentrations on the elongation of segments of sunflower hypocotyl. Ordinate, increase in length, in millimeters; abscissa, time, in hours. (△) Coumarin, 10 ppm; (×) coumarin, 100 ppm; (▲) coumarin, 500 ppm; (●) coumarin, 1000 ppm; (○) water.

straight-growth test or the split pea test (*4*), though in low concentrations ($10^{-5}M$ to $10^{-3}M$) it acts synergistically with indoleacetic acid. In the course of an investigation of the latter effect in sunflower hypocotyls I have observed that coumarin is itself a strong promoter of elongation.

The experiments described in this report were carried out on *Helianthus*, variety Pole Star. Seedlings were grown in vermiculite at 26°C in the dark. One-centimeter sections of the hypocotyl, taken about 1 cm below the cotyledonary node of 6-day-old plants, were placed in the solutions to be tested in red light. The subsequent increase in length of the sections was determined under a binocular dissecting microscope with a micrometer scale.

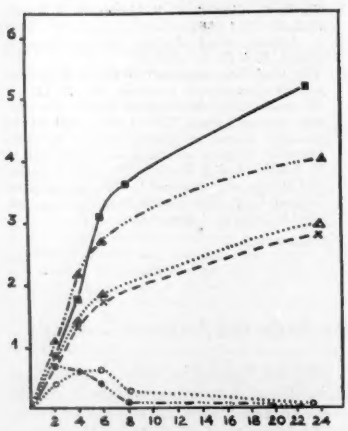

Fig. 2. The effect of coumarin and of 4-hydroxycoumarin on the elongation of segments of sunflower hypocotyl. Ordinate, increase in length, in millimeters; abscissa, time, in hours. (■) Coumarin, 250 ppm; (○) 4-hydroxycoumarin, 250 ppm; (△) 4-hydroxycoumarin, 50 ppm; (●) coumarin, 250 ppm, plus 4-hydroxycoumarin, 250 ppm– (▲) coumarin, 250 ppm, plus 4-hydroxycoumarin, 50 ppm; (×) water.

It was found, when a comparison was made with controls placed in water, that coumarin very markedly stimulated elongation of the sections. Measurements made after 24 hours indicated that the magnitude of the stimulation was related to the concentration of coumarin, the optimum curve resembling that for stimulation induced by auxins. Maximum stimulation was produced by a concentration of coumarin of about 250 parts per million. Measurements made after shorter time intervals, however, revealed that even the supraoptimal concentrations of coumarin strongly stimulated growth during the first few hours; there was then a decline in rate of elongation (see Fig. 1). The sharpness of this decline increased with increase in coumarin concentration.

Previous workers (*2, 3*) have investigated the relation between the structure and the activity of coumarin and its derivatives. Usually, alteration of the coumarin molecule caused a decrease in the effect on germination and root growth. In the investigation reported here, the effect of substitution was found to be greatest in positions 3 and 4, adjacent to the unsaturated bond of the lactone ring. As measured after 24 hours, the increase in length of segments in 250-ppm solutions of coumarin, 4-hydroxycoumarin, 3-chlorocoumarin and 3-methylcoumarin was 295, 0, 120, and 130 percent, respectively (relative to 100 percent in water). Application of 4-hydroxycoumarin in concentrations which did not inhibit elongation partly abolished the stimulating effect of coumarin when the two compounds were applied together (Fig. 2). The effect of substitution demonstrated here for hypocotyl elongation is considerably more marked than that reported for seed germination (*2*) and root growth (*3*).

The growth-promoting effect of coumarin is not confined to *Helianthus* hypocotyls. It has also been observed in preliminary experiments with *Avena* coleoptiles (see *5*), *Pisum* epicotyls, and *Phaseolus* hypocotyls. This activity, when considered in conjunction with the fact that coumarin in the concentrations usually applied inhibits root growth but at very low concentrations may stimulate it (*6*), suggests that this substance should be regarded as a naturally occurring growth regulator (*7*).

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20 February 1959

Antidromic Cortical Response to Stimulation of Isolated Pyramidal Tract

Abstract. Direct electrical excitation of the intact medullary pyramids evokes a complex cortical response. When the pyramidal tract was dissected away from the bulb and stimulated in isolation, the antidromic cortical response consisted of a simple, positive potential, regardless of the stimulus parameters. This finding necessitates a reinterpretation of previous results obtained by stimulation of the intact pyramids.

Stimulation of the medullary pyramids has been widely used to study the behavior of various parts of Betz cells (*1*)—for example, apical dendrites, recurrent collaterals and others—and to map the origin of the corticospinal tract. Studies purporting to demonstrate ascending fibers in the medullary pyramids have proved to be in error because of the spread of current to adjacent ascending fibers (*2*). It appears that several other results obtained by antidromic pyramidal stimulation need to be reviewed in the light of the following experiments (*3*).

The bulbar pyramids and the anterior cerebral hemispheres were exposed in cats anesthetized with α-chloralose (35 mg/kg, intraperitoneal) and paralyzed with decamethonium bromide (1 mg/hr, intravenous). The preparation was placed supine, and bipolar silver-wire electrodes were placed on one exposed pyramid. Monopolar surface recordings were made from the ipsilateral pericruciate cortex. Stimulation of the intact pyramid yielded the cortical potential shown in Fig. 1*A*. The positive (downward) wave *a* (latency, 0.4 to 0.6 msec; duration, 1 msec) had the lowest threshold, faithfully followed repetitive shocks

in excess of 200 per second, and survived longest following death by asphyxiation. This wave is due to antidromic conduction in Betz cell axons. Wave *b* (latency, 1.5 msec; duration, 1–2 msec) was usually monophasically positive and had a higher threshold than wave *a*. Wave *b* was unaltered at stimulus rates up to 20 to 30 per second but decreased at higher rates and failed completely at 80 to 100 shocks per second. This component was also attenuated by prior shocks to the contralateral forepaw. The interpretation of *b* is still uncertain. Components *c* and *d* were highly variable, wave *c* (latency, 3 to 5 msec; duration, 4 to 5 msec) being sometimes positive and sometimes positive-negative in configuration, and *d*, which immediately followed *c*, being similar to the primary cortical response following stimulation of the contralateral forepaw. Waves *c* and *d* both interacted strongly with the primary cortical response, the time-course of the interaction being approximately that of a primary cortical response similarly conditioned. Increasing the intensity or duration, or both, of the stimulus recruited the components sequentially from *a* to *d*; however, *b*, *c*, and *d* differed only slightly in threshold. Gradually increasing the frequency of repetitive stimulation sequentially eliminated the components from *d* to *b*, leaving *a* unaltered.

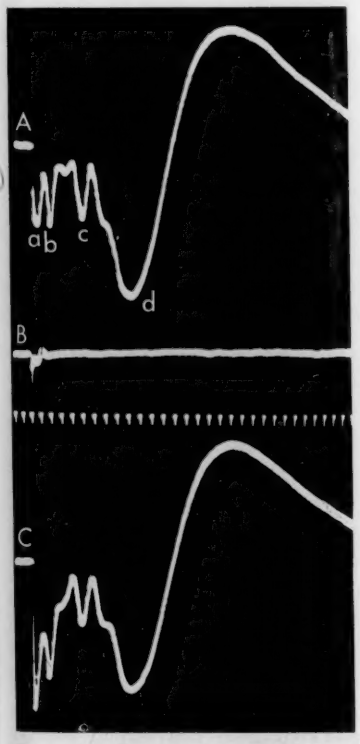

Fig. 1. (*A*) Response from lateral tip of cruciate fissure following stimulation of intact medullary pyramid. (*B*) Response from same point following stimulation of isolated pyramidal strand; *a* wave is 25 μv peak-to-peak. This record shows the greatest negativity in the *a* wave that was ever observed and is among the smallest isolated responses observed. (*C*) Response after contact of strand with brain stem. The slow component of the shock artifact is larger in *C* than in *A*. Time, 1 msec. Shocks were 50 v square pulses of 0.05-msec duration, led through an isolation transformer.

After these observations, the pia mater was dissected away from the ventral medullary surface. A section of pyramidal tract approximately 3 mm long and less than 1 mm in diameter was cut transversely at its caudal end. This strand was then lifted onto bipolar electrodes, free from the underlying bulbar tissue. Such isolation reduced to negligible proportions any spread of stimulating current to structures outside the strand. Stimulation of this isolated strand produced the response shown in Fig. 1*B*. This response consisted of a positive potential which was identical in properties to component *a*, except that the threshold was slightly elevated. This positive wave was sometimes followed by a brief (0.5 msec) negative wave and a prolonged positive wave, both of exceedingly small amplitude. The amplitude of the *a* wave (20 to 120 μv) varied from one preparation to another according to the amount of pyramid included in the strand. That loss of viability of the strand was not responsible for the absence of *b*, *c* and *d* was indicated by the fact that the strand conducted the direct and indirect pyramidal discharges from cortical stimulation (*4*) and the reflex corticofugal discharge (*5*) from stimulation of the contralateral forepaw. Increased strength (up to 50 v) or pulse duration (up to 1 msec), or repetition (up to 500 per second for 5 sec) of the stimulus did not alter the response seen in Fig. 1*B* except in amplitude. When the electrodes carrying the strand were lowered into contact with the underlying bulbar tissue, the fully developed complex reappeared (Fig. 1*C*).

At the end of each experiment, the animal was perfused with formalin, and the bulb was removed, serially sectioned, and Luxol-fast or Weil stained to determine the amount of pyramidal tract dissected (Fig. 2). Evidently stimulation of the intact medullary pyramids excites a host of elements in addition to pyramidal axons. Component *d* has generally been recognized as resulting from spread of the stimulus to adjacent corticopetal fibers of the medial lemniscus,

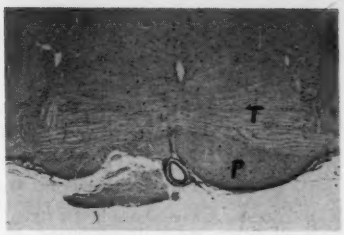

Fig. 2. Luxol-fast section through bulbar pyramid showing extent of dissection; this dissected strand is larger than usual: *P*, intact pyramid; *T*, trapezoid body. Medial lemniscal fibers are interspersed through the trapezoidal fibers and between the pyramid and trapezoid body.

but the first three components have been regarded as the cortical consequence of activity in pyramidal fibers exclusively. The experiment reported here leads to the conclusion that the sole cortical consequence of antidromic pyramidal activation is the *a* wave (and, perhaps, the inconstant, prolonged positive potential of extraordinarily minute amplitude following the *a* wave). The prominent *b* wave and the variable *c* wave must result from activation of hitherto unsuspected elements in the vicinity of the medullary pyramidal tracts.

Such a finding calls for a reevaluation of those studies in which antidromic stimulation has been used in an attempt to map the cortical origin of the pyramidal tract (*6*) and of many other experiments depending upon the original interpretation of the antidromic potential (*7*). Stimulation of the isolated pyramidal strand fails to yield a large, prolonged surface-negative potential; such a potential, which is observed when the intact pyramidal surface is stimulated, has been ascribed to activity in apical dendrites (*8, 9*). Moreover, the concept of recurrent collateral activation of apical dendrites directly or via interneurons does not find any support (*9, 10*); no delayed activity could be detected following stimulation of the strand.

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15 April 1959

Effect of Diisopropylfluorophosphate on Sulfhydryl Proteases

Abstract. Diisopropylfluorophosphate inhibited all the sulfhydryl proteases studied in our tests. This inhibition was most pronounced at *p*H 6.0. By first blocking the sulfhydryl group with *p*-chloromercuribenzoate, inhibition could be prevented. Neither cysteine nor choline gave appreciable reactivation of diisopropylfluorophosphate-inhibited bromelain.

Although the organic phosphate nerve gases are well established as specific inhibitors of certain esterases, trypsin and chymotrypsin, activated plasmin and phosphoglucomutase (*1*), no reports of specific inhibition of the sulfhydryl enzymes have been made (*2*).

In a comparative study of plant proteases we found that moderate concentrations of diisopropylfluorophosphate inhibited many preparations of bromelain (*3*), papain, and ficin. With commercial bromelain, $4 \times 10^{-4}M$ diisopropylfluorophosphate inhibited 50 percent of the protease activity within 2 hours at room temperature. Some of our fractionated bromelain preparations, on the other hand, showed only slight inhibition at high concentrations of reagent.

The effectiveness of diisopropylfluorophosphate as an inhibitor depended not only on the type of enzyme and the degree of purity of the enzyme but also on the *p*H of the solution (Fig. 1). Bromelain and papain, which presumably have similar active sites, showed an entirely different behavior at all *p*H values below *p*H 5.0. On the other hand, Rhozyme P-11, a fungal protease which does not require a free sulfhydryl group for enzymatic activity, showed a *p*H-inhibition curve which was remarkably similar to that of bromelain. These similarities and differences may provide clues to the nature of the active sites on these enzymes, or to the effect of unknown materials in these preparations which mediates the action of diisopropylfluorophosphate on sulfhydryl groups.

That the sulfhydryl group is the site actually being affected is shown by an experiment summarized in Table 1. Blocking the sulfhydryl group with *p*-chloromercuribenzoate before exposing the enzyme to diisopropylfluorophosphate gave complete protection against inhibition. Another sulfhydryl blocking technique, and one which may frequently occur with enzyme preparations, is mild oxidation. This also protected against diisopropylfluorophosphate.

Attempts to reactivate diisopropylfluorophosphate-inhibited bromelain with cysteine, choline, or a combination of the two reagents at either *p*H 5.0 or *p*H 7.0 have been only slightly successful. Cysteine regenerated no more than 10 percent of the original activity.

Our finding that diisopropylfluorophosphate, under the proper conditions, will react with sulfhydryl enzymes now makes this chemical a fairly general protein reagent. It will react directly with the nitrogen of imidazole or the hydroxyl of tyrosine (*4*); it will react directly or indirectly with amino (*5*) and sulfhydryl groups; it will react indirectly with the hydroxyl group of serine (*1*, *6*).

Table 1. Effect of protecting the sulfhydryl group of a purified bromelain sample on inactivation by diisopropylfluorophosphate (DFP).

Treatment	Milk-clotting unit*/g	Percentage of 4660
Enzyme in *p*H 7.0 buffer (no PCMB)†	4660	100
Enzyme in 25 percent isopropylalcohol (IPA)	4520	97
Assayed without cysteine after dialysis	2620	56
Assayed with 0.005*M* cysteine after dialysis	4500	97
Enzyme in 25 percent IPA with $10^{-3}M$ DFP	706	15
Assayed without cysteine after dialysis	52	1
Assayed with 0.005*M* cysteine after dialysis	450	10
Enzyme in *p*H 7.0 buffer with PCMB†	80	2
Enzyme in 25 percent isopropylalcohol	0	0
Assayed without cysteine after dialysis	552	12
Assayed with 0.005*M* cysteine after dialysis	4900	105
Enzyme in 25 percent IPA with $10^{-3}M$ DFP	0	0
Assayed without cysteine after dialysis	486	10
Assayed with 0.005*M* cysteine after dialysis	4900	105

* Milk-clotting unit: 1 min to clot 5 ml of a 5-percent skim milk solution adjusted to *p*H 5.3 and incubated at 37.5°C. † *p*-Chloromercuribenzoate.

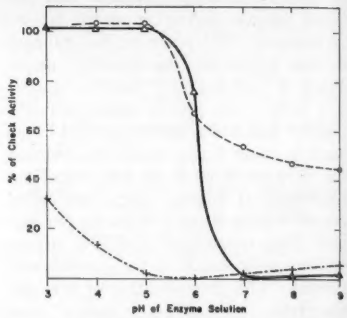

Fig. 1. Effect of *p*H on the inhibition of bromelain (solid line), papain (dashed line with crosses), and Rhozyme P-11 (dashed line with circles) by diisopropylfluorophosphate. The enzymes were incubated for 1 hour at 25°C in $1 \times 10^{-3}M$, $1 \times 10^{-3}M$, and $1 \times 10^{-4}M$ diisopropylfluorophosphate, respectively.

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3 November 1958

Influence of Adrenalectomy and Hypophysectomy on Cerebral Serotonin

Abstract. Changes in serous and encephalic serotonin in hypophysectomized or adrenalectomized rats have been observed. Adrenalectomy produces a decrease of serous serotonin and an increase of the serotonin of hemispheres, base, and medulla oblongata; with hypophysectomy, serotonin is also reduced in serum and increased only in the base and medulla oblongata.

It is known that the cerebral serotonin content can be varied by artificial means, either by stimulating the formation of

serotonin through administration of precursor drugs such as 5-hydroxytryptophan (*1*), or by preventing its degredation, by means of iproniazid, which is an excellent inhibitor of monoaminooxidase (*2*). It is also known that the administration of suitable doses of reserpine causes a reduction in the encephalic serotonin and a considerable increase in the urinary excretion of 5-hydroxyindoleacetic acid, the most important metabolite of serotonin (*3*). Chlorpromazine, meprobamate, and benactizine, on the other hand, have only slight or no effect on urinary elimination of 5-hydroxyindoleacetic acid (*4*).

I have also considered another powerful tranquilizer, hydroxyzine hydrochloride (Atarax), about which Zubiani and I have published a complete clinical study (*5*). At the present time I am studying its influence on serotonin metabolism in man (blood and cerebrospinal fluid) and in animals (blood and brain).

This preliminary note reports the modifications in encephalic and serous serotonin that have been observed in whole rats after adrenalectomy and hypophysectomy.

Sixty white rats, each weighing 200 to 250 g, were divided into three groups of 20 each. The first group was left untreated and served as controls; the second group underwent bilateral adrenalectomy; and the third, hypophysectomy. This was carried out by the transpharyngeal route. The complete removal of the hypophysis was later verified by autopsy. The animals were killed by decapitation 24 hours after the operation. The brain, which was immediately removed, was divided into four portions consisting of the hemispheres, the base, the medulla oblongata, and the cerebellum. The brain portions were then subjected to the following treatment: extraction with 80-percent acetone and filtration after 24 hours; replacement of the acetone by a fresh batch of 80-percent (5 volumes); further filtration after a second 24 hours; combination of the two filtrates and evaporation of the acetone; making up to volume with Tyrode's solution containing atropine. The serum was subjected to: extraction with 2 volumes of 100-percent acetone; filtration after 24 hours; and making up to volume with Tyrode's solution containing atropine.

Table 1. Serotonin values, in micrograms per 100 g of tissue, found in various locations in control, adrenalectomized, and hypophysectomized rats. The figures in parentheses are the percentage difference from the values found for the control rats.

No.	Rats	Location				
		Serum	Hemispheres	Base	Medulla oblongata	Cerebellum
20	Controls	50	85	97	37	0
20	Adrenalectomized	12 (– 76)	195 (+ 129)	115 (+ 18)	140 (+ 278)	0
20	Hypophysectomized	20 (– 60)	87 (+ 2)	154 (+ 58)	81 (+ 118)	0

For quantitative assay of the serotonin, I used rat uterus in estrus, according to Erspamer's technique (*6*). The values of encephalic and serous serotonin are expressed in micrograms per 100 g of fresh tissue.

In the control rats, the encephalic serotonin was found to be present in the quantity of 85 μg for the hemispheres, 97 μg for the base, and 37 μg for the medulla oblongata. Fifty micrograms were found in the blood serum. No trace of serotonin was found in the cerebellum, and this result agrees with the published literature. Adrenalectomized rats gave the following values for serotonin 24 hours after operation: 195 μg for the hemispheres, 115 μg for the base, 140 μg for the medulla oblongata, and 12 μg for the serum. In the hypophysectomized rats, 24 hours after operation, assay of the serotonin revealed values of 87 μg for the hemispheres, 154 μg for the base, 81 μg for the medulla oblongata, and 20 μg for the serum. These results are summarized in Table 1.

It is thus seen that adrenalectomy led to marked changes in the cerebral serotonin, which was constantly and significantly increased in the hemispheres, base and medulla oblongata, with increases of 129, 18, and 278 percent respectively, in comparison with the controls. Hypophysectomy caused a large increase in serotonin only in the base (58 percent) and the medulla oblongata (118 percent). The concentration of serotonin in the hemispheres remained practically unchanged. In both groups of animals that underwent surgical treatment, the highest increase was observed in the medulla oblongata. Both hypophysectomy and adrenalectomy produced a large reduction in the serous serotonin, which fell by 60 percent in hypophysectomized rats and 76 percent in adrenalectomized animals.

I therefore feel that it is too early to attempt to give an explanation of these results. They do, however, point to the importance of a study of the relationships between serotonin and endocrine glands (particularly the adrenals) on one hand, and mental diseases (particularly schizophrenia) on the other.

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6 August 1958

Meetings

Society in the Ancient Near East

On 4–7 Dec. 1958, a symposium was held in the Oriental Institute of the University of Chicago, on "The Expansion of Society in the Ancient Near East and its Cultural Implications." There were some 70 invited participants, of whom 20 represented other institutions in this country and institutions abroad. About half of the group were scholars whose competence lay in the natural and social sciences and in the culture-historical sequences of areas other than those of the ancient Near East. The remainder of the group consisted of specialists in the archeology, philology, and culture-history of the eastern end of the Mediterranean in pre-Greek, Greco-Roman, and Islamic times.

The symposium included a series of general background papers prepared by Robert M. Adams, Robert J. Braidwood, Mircea Eliade, I. J. Gelb, David Grene, G. E. von Grunebaum, Clyde Kluckhohn, Karl Polanyi, Max Rheinstein, Otto von Simson, and Milton Singer, respectively. There were introductory and concluding addresses by Lewis Mumford. The six sessions dealt with the background for the expansion of society in the alluvium and the upland of the Near East, with the development of culture in the national states, and with the development of cultures in the great empires. Discussion leaders included R. M. Adams, N. Glueck, I. P. H. Jacobsen, B. Landsberger, J. A. Wilson, H. Guterbock, and C. H. Kraeling.

It has been traditional for scholars concerned with the ancient Near East to restrict their studies to their own area of competence. The success of the symposium rested in fair part on the fact that these traditional scholarly concerns were communicated to and drew fruitful discussion from interested colleagues in the natural and social sciences and from culture-historians concerned with other areas of the Old and New Worlds. As the symposium progressed, the expansion of society and the appearance and development of urban civilization in the ancient Near East came to be seen against a broad background of general phenomena in both natural and cultural history.

Given the present order of incompleteness of knowledge, it was natural that there were more new problems raised than old problems solved. The importance of the symposium rests in its success as a means of bringing about cross-disciplinary communication. The proceedings of the symposium will be published by the Oriental Institute as soon as practicable.

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Pan American Medical Congress to Include Space-Medicine Section

The next congress of the Pan American Medical Association, 745 Fifth Ave., New York 22, N.Y., is to be held in Mexico City, from 2 May to 11 May 1960. Some 5000 physicians from the 22 American nations are expected to attend. The scientific program of the congress, through its 48 different medical sections, will include all branches of medicine and surgery; also a section on dentistry. The congress will also have scientific and commercial exhibits, panels on special subjects, medical motion pictures, and closed-circuit television demonstrations of surgical and dental techniques. There will be some new sections, such as a section on hematology, a section on general medical practice, and—of special interest—a section on space medicine.

Major General Otis O. Benson, Jr., commandant of the School of Aviation Medicine, Randolph Air Force Base, Tex., has been named president of the space-medicine section, and S. Fred Singer, professor of physics at the University of Maryland, is secretary. The Latin American chairman of the section is Col. Raul Terres y Prieto, M.C.,

surgeon general of the Mexican Air Force, while Brig. Gen. Donald D. Flickinger, staff surgeon and director of life sciences, Air Research and Development Command, is North American chairman.

Semiconductor Surfaces

A conference on semiconductor surfaces will be held at the U.S. Naval Ordnance Laboratory, White Oak, Silver Spring, Md., 3–4 December, under the sponsorship of NOL and the Office of Naval Research. Papers are invited on the following subjects: clean germanium and silicon surfaces, etched and chemically treated germanium and silicon surfaces, theory of surface properties, surface chemistry, and new experimental approaches. The proceedings will be published. Those interested in attending the conference or in submitting papers may write for information to the chairman of the steering committee, Dr. J. N. Zemel, U.S. Naval Ordnance Laboratory, White Oak, Silver Spring, Md.

Summer Biological Symposium

"Cell Structure and Function" will be the theme of the tenth annual Biological Symposium, to be held 6–8 July at the University of Michigan under the auspices of the division of biological sciences. Five prominent scientists from this country and abroad have been invited to discuss their recent work in this field. They are S. Granick and George E. Palade of the Rockefeller Institute for Medical Research; H. E. Huxley of the department of biophysics, University College, London; Hans Ris of the Department of zoology, University of Wisconsin; and C. F. Robinow of the Faculty of Medicine, University of Western Ontario. For information about housing and other details, communicate with Dr. John M. Allen of the Department of Zoology, University of Michigan, Ann Arbor, Mich.

Forthcoming Events

July

19–24. American Crystallographic Assoc., Ithaca, N.Y. (J. Waser, Rice Inst., Houston 5, Tex.)

19–25. Pediatrics, 9th intern. cong., Montreal, Canada. (R. L. Denton, P.O. Box 215, Westmount, Montreal 6.)

20–26. Radiation and Atmospheric Ozone, joint symp., by Intern. Union of Geodesy and Geophysics and World Meteorological Organization, Oxford, England. (WMO, Campagne Rigot, 1, avenue de la Paix, Geneva, Switzerland.)

22–23. Rocky Mountain Cancer Conf., Denver, Colo. (N. Paul Isbell, 835 Republic Bldg., Denver 2.)

23–30. Radiology, 9th intern. cong., Munich, Germany. (Sekretariat des 9 Internationalen Kongresses für Radiologie, Reitmorstrasse 29, Munich 22.)

26–30. International Psychoanalytical Assoc., Copenhagen, Denmark. (Miss P. King, 37 Albion St., London, W.2,

27–4. International Federation of Translators, Bad Godesberg, Germany. (Dritter Internationaler FIT-Kongress, Kongress Sekretariat, Bundesverband der Dolmetscher und Übersetzer e. V. (BDÜ) Hausdorfstrasse 2, Bonn, Germany.)

30–31. Computers and Data Processing, 6th annual symp., Estes Park, Colo. (W. H. Eichelberger, Denver Research Inst., Univ. of Denver, Denver 10, Colo.)

August

1–8. World Congress of Esperantists, 44th, Warsaw, Poland. (Office of Intern. Conferences, Dept. of State, Washington 25.)

4–5. American Astronautical Soc., 2nd annual western, Los Angeles, Calif. (A. P. Mayernik, AAS, 6708 53 Rd., Maspeth 78, N.Y.)

6–8. Human Pituitary Hormones, colloquium (by invitation only), Buenos Aires, Argentina. (G. E. W. Wolstenholme, Ciba Foundation, 41 Portland Place, London W.2, England.)

9–12. American Soc. of Mechanical Engineers (Heat Transfer Div.), conf., Storrs, Conn. (D. B. MacDougall, ASME, 29 West 39 St., New York 18.)

9–15. Physiological Sciences, 21st intern. cong., Buenos Aires, Argentina. (C. F. Schmidt, Univ. of Pennsylvania School of Medicine, Philadelphia 4.)

10–13. National Medical Assoc., Detroit, Mich. (J. T. Givens, 1108 Church St., Norfolk, Va.)

10–13. Society of Automotive Engineers, natl. West Coast meeting, Vancouver, B.C., Canada. (R. W. Crory, Meetings Operation Dept., SAE, 485 Lexington Ave., New York 17.)

16–19. Botanical Nomenclature, discussions (Intern. Bureau for Plant Taxonomy and Nomenclature), Montreal, Canada. (J. Rousseau, Natl. Museum, Ottawa, Canada.)

16–21. American Pharmaceutical Assoc., Cincinnati, Ohio. (R. P. Fischelis, APA, 2215 Constitution Ave., NW, Washington 7.)

17. Ultrasonics, natl. symp., San Francisco, Calif. (L. G. Cumming, Inst. of Radio Engineers, 1 E. 79 St., New York 21.)

17–21. Pacific Southwest Assoc. of Chemistry Teachers, Pacific Grove, Calif. (W. A. Craig, 416 N. Citrus Ave., Los Angeles 36, Calif.)

17–22. Logopedics and Phoniatrics, 11th intern. cong., London, England. (Miss P. Carter, 46 Canonbury Square, London N.1, England.)

19–26. Refrigeration, 10th intern. cong., Copenhagen, Denmark. (M. Kondrup, Danish Natl. Committee, Intern. Congress of Refrigeration, P.O. Box 57, Roskilde, Denmark.)

19–29. Botanical Cong., 9th intern., Montreal, Canada. (C. Frankton, Secretary-General, 9th Intern. Botanical Cong., Science Service Bldg., Ottawa, Ontario, Canada.)

19–29. International Assoc. of Wood Anatomists, Montreal, Canada. (IAWA, Laboratorium für Holzforschung E.T.H. Universitatstrasse 2, Zurich, Switzerland.)

19–29. Mycological Soc. of America, Montreal, Canada. (E. S. Beneke, Dept. of Botany and Plant Pathology, Michigan State Univ., E. Lansing.)

19–29. Phycological Soc. of America, Montreal, Canada. (W. A. Daily, Dept. of Botany, Butler Univ., Indianapolis 7, Ind.)

20–22. Rocky Mountain Radiological Soc., Denver, Colo. (J. H. Freed, 4200 E. Ninth Ave., Denver 20.)

20–25. Chemical Thermodynamics, symp., Wattens, Austria. (F. Vorländer, Deutsche Bunsen-Gesellschaft, Carl-Bosh-Haus, Varrentrappstrasse, 40–42, Frankfort a.M., Germany.)

20–27. Therapeutics, symp., Gardone, Italy. (R. Morf, c/o Sandoz S.A., Basel 13, Switzerland.)

20–2. Limnological Cong., 14th intern., Vienna and Salzburg, Austria. (Secretary, 14th Intern. Limnological Congress, Biologische Station, Lunz am See, Austria.)

23–26. American Farm Economic Assoc., Ithaca, N.Y. (C. D. Kearl, Dept. of Agricultural Economics, Warren Hall, Cornell Univ., Ithaca.)

23–27. Veterinary Medicine, 3rd Pan-American Cong., Kansas City, Mo. (B. D. Blood, Pan-American Congresses of Veterinary Medicine, P.O. Box 99, Azuk, Buenos Aires Province, Argentina.)

24–26. American Accounting Assoc., Boulder, Colo. (C. Cox, 437 Hagerty Hall, Ohio State Univ., Columbus 10.)

24–26. Anti-Submarine Warfare (classified), symp., San Diego, Calif. (R. R. Dexter, Inst. of the Aeronautical Sciences, 2 E. 64 St., New York 21.)

24–26. Dynamics of Conducting Fluids, (American Rocket Soc., and Northwestern Univ.), Evanston, Ill. (J. J. Harford, ARS, 500 Fifth Ave., New York 36.)

24–27. American Hospital Assoc., New York, N.Y. (E. L. Crosby, 18 E. Division St., Chicago, Ill.)

24–28. Australian and New Zealand Assoc. for the Advancement of Science, 34th cong., Perth, Western Australia. (J. R. A. McMillan, Science House, 157 Gloucester St., Sydney, Australia.)

24–29. Infrared Spectroscopy Inst., 10th annual, Nashville, Tenn. (N. Fuson, Director, Infrared Spectroscopy, Fisk Univ., Nashville 8.)

24–29. International Assoc. for Hydraulic Research, cong., Montreal, Canada. (IAHR, c/o Laboratoire Hydraulique, Raam 61, Delft, Netherlands.)

24–29. Ionization Phenomena in Gases, 4th intern. conf., Upsala, Sweden. (A. Nilsson, Secretary-General, Inst. of Physics, Upsala, Sweden.)

24–29. Polarography, 2nd intern. cong., Cambridge, England. (Mrs. B. Lamb, Chemistry Lab., Evershed & Vignoles, Corner of Iveagh Ave., N. Circular Rd., London N.W.10, England.)

24–30. Modern Systems for Detecting and Evaluating Optical Radiation (Intern. Optical Commission), symp., Stockholm, Sweden. (S. S. Ballard, Dept. of Physics, Univ. of Florida, Gainesville.)

25–27. Petroleum Industry Conf., AIEE, Long Beach, Calif. (N. S. Hibshman, AIEE, 33 W. 39 St., New York 18.)

25–28. Alaskan Science Conf., Alaskan Div., AAAS, 10th, Juneau. (N. J. Wilimovsky, Bur. of Commercial Fisheries, Box 2021, Juneau.)

25–28. American Dietetic Assoc., 42nd annual, Los Angeles, Calif. (Miss R. M. Yakel, ADA, 620 N. Michigan Ave., Chicago 11, Ill.)

25–30. American Ornithologists' Union, Regina, Saskatchewan, Canada. (H. G. Deignan, Div. of Birds, U.S. National Museum, Washington 25.)

26–29. International Assoc. of Milk and Food Sanitarians, Glenwood Springs, Colo. (V. T. Foley, Health Dept., Kansas City, Mo.)

26–29. International Union of Pure and Applied Chemistry, 20th conf., Munich, Germany. (Div. of Chemistry and Chemical Technology, Natl. Research Council, Washington 25.)

27–29. American Assoc. of Clinical Chemists, 11th annual, Cleveland, Ohio. (A. Hainline, Jr., AACC, Cleveland Clinic Foundation, 2020 E. 93 St., Cleveland 6.)

27–29. American Physical Soc., Hawaii. (K. K. Darrow, APS, Columbia Univ., New York 27.)

28–29. Weather Modification (with American Soc. of Civil Engineers), conf., Denver, Colo. (H. G. Houghton, AMS, Dept. of Meteorology, Massachusetts Inst. of Technology, Cambridge 39, Mass.)

28–30. American Folklore Soc., annual, Albany and Cooperstown, N.Y. (MacE. Leach, 110 Bennett Hall, Univ. of Pennsylvania, Philadelphia 4.)

28–31. Astronomical League, Denver, Colo. (R. Dakin, 720 Victor Rd., Pittsford, N.Y.)

28–4. International Union for Scientific Study of Population, cong., Vienna, Austria. (F. Lorimer, Dept. of Sociology, American Univ., Washington, D.C.)

30–3. American Inst. of Biological Sciences, annual, University Park, Pa. (H. T. Cox, AIBS, 2000 P St., NW, Washington 6.)

The following 17 meetings are being held in conjunction with the AIBS meeting at University Park, Pa.

American Microscopical Soc. (T. H. Cheng, Dept. of Zoology and Entomology, Pennsylvania State Univ., University Park.)

American Phytopathological Soc. (J. E. Livingston, Dept. of Botany and Plant Pathology, Pennsylvania State Univ., University Park.)

American Soc. for Horticultural Science. (R. E. Larson, Dept. of Horticulture, Pennsylvania State Univ., University Park.)

American Soc. of Human Genetics. (C. C. Li, Graduate School of Public Health, Univ. of Pittsburgh, Pa.)

American Soc. of Limnology and Oceanography. (E. L. Cooper, Dept. of Zoology, Pennsylvania State Univ., University Park.)

American Soc. of Parasitologists. (T. H. Cheng, Dept. of Zoology and Entomology, Pennsylvania State Univ., University Park.)

American Soc. of Plant Physiologists. (A. A. Benson, Agriculture and Biological Chemistry, Pennsylvania State Univ., University Park.)

American Soc. of Zoologists. (A. Anthony, Dept. of Zoology, Pennsylvania State Univ., University Park.)

Biometric Soc. (ENAR). (Miss C. S. Weil, Mellon Inst., 4400 Fifth Ave., Pittsburgh, Pa.)

Ecological Soc. of America. (M. W. Schein, Dept. of Poultry Husbandry, Pennsylvania State Univ., University Park.)

Genetics Soc. of America. (J. E. Wright, Dept. of Genetics, Pennsylvania State Univ., University Park.)

National Assoc. of Biology Teachers. (H. S. Fowler, Science Education, Pennsylvania State Univ., University Park.)

Nature Conservancy. (W. Sharp, Pennsylvania Cooperative Wildlife Reserve, 206 Forestry Bldg., Pennsylvania State Univ., University Park.)

Society for Industrial Microbiology. (Miss M. B. O'Hara, Applied Sciences Labs., Inc., State College, Pa.; or A. Rose, 525 S. Gill St., State College.)

Society of Protozoologists. (H. Frings, Dept. of Zoology, Pennsylvania State Univ., University Park.)

Society for the Study of Development and Growth. (J. E. Livingston, Dept. of Botany and Plant Pathology, Pennsylvania State University, University Park.)

Tomato Genetics Cooperative. (B. L. Pollack, Dept. of Horticulture, Pennsylvania State Univ., University Park.)

30–4. American Cong. of Physical Medicine and Rehabilitation, Minneapolis, Minn. (Miss D. C. Augustin, 30 N. Michigan Ave., Chicago 2, Ill.)

30–4. Laurentian Hormone Conf., Mont Tremblant, Quebec, Canada. (G. Pincus, 222 Maple Ave., Shrewsbury, Mass.)

30–4. Medical Education, 2nd world conf., Chicago, Ill. (World Medical Assoc., 10 Columbus Circle, New York 19.)

30–5. World Federation for Mental Health, 12th annual, Barcelona, Spain. (Miss E. M. Thornton, Secretary-General, WFMH, 19, Manchester St., London W.1, England.)

30–6. History of Science, 9th intern. cong., Barcelona and Madrid, Spain. (J. Vernet, via Layetona 141, Barcelona.)

30–6. Residues on Crops and/or the Problem of Insect Resistance to Insecticides, symp., Munich, Germany. (R. Morf, Secretary-General, IUPAC, c/o Sandoz S. A., Basel, Switzerland.)

30–6. Thermodynamics and Experimental Thermochemistry, 17th intern. cong. (Intern. Union of Pure and Applied Chemistry), Munich, Germany. (Div. of Chemistry and Chemical Technology, Natl. Research Council, Washington 25.)

31–2. Stratospheric Meteorology, conf., Minneapolis, Minn. (H. G. Houghton, AMS, Dept. of Meteorology, Massachusetts Inst. of Technology, Cambridge 39, Mass.)

30–12. International Oceanographic Cong. (AAAS, UNESCO, ICSU), New York, N.Y. (Miss M. Sears, chairman, Woods Hole Oceanographic Institution, Woods Hole, Mass.)

31–2. Free Radical Stabilization, 4th intern. symp., Washington, D.C. (A. M. Bass, Natl. Bureau of Standards, Washington 25.)

31–3. Biological Photographic Assoc., Montreal, Canada. (Miss J. H. Waters, P.O. Box 1668, Grand Central Station, New York 17.)

31–3. Mathematical Assoc. of America, 40th summer meeting, Salt Lake City, Utah. (H. M. Gehman, MAA, Univ. of Buffalo, Buffalo 14, N.Y.)

31–4. Haematin Enzymes, symp. (by invitation), Canberra, Australia. (A. H. Ennar, John Curtin School of Medical Research, Australian National Univ., Canberra.)

September

1–3. Association for Computing Machinery, natl., Cambridge, Mass. (J. Moshman, Council for Economic and Industry Research, Inc., 1200 Jefferson Davis Highway, Arlington 2, Va.)

1–6. College of American Pathologists, Chicago, Ill. (A. H. Dearing, Suite 2115 Prudential Plaza, Chicago 1.)

1–7. History and Philosophy of Science (General Assembly, History Div., Intern. Union of the History and Philosophy of Science), Barcelona, Spain. (R. Taton, IUHPS, 64, rue Gay-Lussac, Paris 5e, France.)

1–8. Acoustics, 3rd intern. cong., Stuttgart, Germany. (E. Zwicker, Breitscheidstrasse 3, Stuttgart N.)

1–7. Oct. International Civil Aviation Organization (Meteorological Div.), Montreal, Canada. (ICAO, Maison de l'Aviation Internationale, Montreal.)

2–4. Allergy, 4th European cong., London, England. (British Assoc. of Allergists, Wright-Fleming Inst., St. Mary's Hospital, London, W.2.)

2–4. Cryogenic Engineering Conf.,

Berkeley, Calif. (K. D. Timmerhaus, CEC, Chemical Engineering Dept., Univ. of Colorado, Boulder.)

2–4. Crystal Imperfections and the Chemical Reactivity of Solids (Faraday discussion), Kingston, Ontario, Canada. (Faraday Soc., 6 Gray's Inn Sq., London, W.C.1, England.)

2–5. American Mathematical Soc. and Mathematical Assoc. of America (joint summer), Salt Lake City, Utah. (E. Pitcher, AMS, Lehigh Univ., Bethlehem, Pa.)

2–8. Foundations of Mathematics: Infinitistic Methods, symp., Warsaw, Poland. (A. Mostowski, Dept. of Mathematics, Univ. of California, Berkeley 4.)

2–9. British Assoc. for the Advancement of Science, 121st annual, York, England. (Secretary, BAAS, 18 Adam St., Adelphi, London, W.C.2, England.)

3–6. American Sociological Soc., natl., Chicago, Ill. (D. Young, Russell Sage Foundation, New York 22.)

3–5. Nephrology, 1st intern. cong., Geneva, Switzerland, and Evian, France. (G. Richet, Hospital Necker, 149, rue de Sevres, Paris 7e, France.)

3–9. American Psychological Assoc., annual conv., Cincinnati, Ohio. (R. W. Russell, APA, 1333 16 St., NW, Washington 6.)

4–7. International Federation of Surveyors, annual (by invitation), Gracow, Australia. (IFS, 4, Kanaalweg, Delft, Netherlands.)

5–11. Application of Radiation Sources in Industry, intern. conf., Warsaw, Poland. (P. Fent, IAEA, Vienna, Austria.)

6–12. Standards on a Common Language for Machine Searching and Translation, intern. conf., Cleveland, Ohio. (Secretariat, Center for Documentation and Communication Research, Western Reserve Univ., Cleveland 6.)

6–12. World Confederation for Physiotherapy, 3rd intern. cong., Paris, France. (A. Nicolle and J. Dupuis-Deltor, Société d'Organisation des Congrès Français et Internationaux, 1, rue Chanez, Paris 16e.)

7–9. Psychometric Soc., Cincinnati, Ohio. (P. H. DuBois, Washington Univ., St. Louis 5, Mo.)

7–9. Society of General Physiologists, Urbana, Ill. (F. G. Sherman, Dept. of Biology, Brown Univ., Providence 12, R.I.)

7–10. Institute of Management Sciences, Paris, France. (A. S. Manne, Dept. of Economics, Yale Univ., New Haven, Conn.)

7–11. American Soc. of Clinical Pathologists, Chicago, Ill. (C. E. Wells, 2052 N. Orleans, Chicago 14.)

7–11. Illuminating Engineering Soc., annual natl. conf., San Francisco, Calif. (A. D. Hinckley, IES,, 1860 Broadway, New York 36.)

7–12. European Soc. of Haematology, cong., London, England. (E. Neumark, Dept. of Pathology, St. Mary's Hospital, London, W.2.)

7–12. World Medical Assoc., 13th general assembly, Montreal, Canada. (WMA, 10 Columbus Circle, New York 19.)

8–15. Sociology, 4th world cong., Milan and Stresa, Italy. (Intern. Sociological Assoc., Skepper House, 13 Endsleigh St., London, W.C.1, England.)

Letters

Scientists Need a Group Opinion

I was pleased by Fletcher Watson's sympathetic and generally favorable review of my book *Science and Education at the Crossroads* [*Science* **129**, 459 (1959)]. One comment of his merits a response. He said that my suggestions "would require marked changes in public opinion; how these could be obtained still eludes many already immersed in the problems."

Watson's statement does not make clear which "public('s) opinion" he refers to. My book was written to help scientists formulate their own scientific (public or group) opinion (about professional policies—*not about scientific matters*) by doing two things: (i) setting up some clear-cut debating topics about "housekeeping" philosophy which could focus discussion, and (ii) describing the "housekeeping" (administrative) machinery that scientists must create to enable them to continuously formulate their own group opinion about scientific and educational policies.

Until these steps are taken, science cannot hope to guide the general public's opinion. At present much of the science and education news the public receives from radio, television or in the press is, or seems to be, mutually contradictory. Information theorists would say that the noise/message ratio is high. Hence the general public gets very little guidance from science to assist it in formulating its opinion. A great deal of this confusion would be reduced if scientists were spending a little more of their time than at present working on their administrative or political "housekeeping" problems. The AAAS has taken some generally correct, but in my opinion still too small, steps toward reaching the goal that United States science needs to reach as rapidly as possible. It's later than we think.

JOSEPH W. STILL
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Doylestown, Pennsylvania

Loyalty Oath

I should like to commend the review in the 6 March issue of *Science* [**129**, 625 (1959)] of recent efforts to rescind the loyalty oath provision of the National Defense Education Act.

I noted with interest the remark that scientists and scientific societies had not yet taken a stand on this issue and that their silence had been attributed to timidity. For the record, I should like to report that at its last meeting in January the Council of the Federation of American Scientists recorded its opposition to this loyalty oath requirement and instructed the executive committee of the FAS to communicate these sentiments to the Congress. Letters supporting repeal of this requirement have been sent to the sponsors of several of the bills that have been introduced for this purpose. In these we have expressed our opposition to the extension of loyalty tests to persons other than those who have access to secret information or who hold positions in which they may by their decisions and actions affect directly and substantially the national security. We have also expressed our particular fear that the antisubversion affidavit requirement in the National Defense Education Act will tend to inhibit free inquiry, association, and exchange of ideas among students and faculty.

AUGUSTUS H. FOX
Federation of American Scientists, Washington, D.C.

What Is a Profession?

In his letter, Hanor A. Webb speaks of two young scientists with majors in chemistry and biology [*Science* **129** 746 (1959)]. He then says: "These young people are specialists but they are not professionals. Professions . . . require certification. . . ."

A profession is determined not by certification but by training, code of ethics, and viewpoint toward the field of the profession. Historically, there are three "learned professions"—medicine, theology and law. Theology is not certified.

Profession is defined in *Webster's New International Dictionary* as "The occupation, if not purely commercial, mechanical, agricultural, or the like, to which one devotes oneself; . . . as, the *profession* of arms, of teaching, of chemist." It is of note here that the profession is "of teaching," not "of education."

The sections of the AAAS are an excellent list of scientific professions: mathematics, physics, chemistry, astronomy, geology, geography, zoology, botany, anthropology, psychology, social sciences, engineering, medicine, agriculture, education. Only three of these require certification, namely, medicine, education and, in some states, engineering. But the certification did not make them professions.

No, a profession requires training, a minimum of not less than four years of college with major work in the field of the profession and minor work in related fields. In addition to the basic college work, experience working either in the profession or for an advanced degree, doing original work, is needed before a person becomes a true professional.

Next, a profession requires a code of ethics either stated or observed in the field. For one such code in the profes-

sion of chemistry (that of the American Institute of Chemists) reference can be made to *The Chemist* [**35**, No. 4, 125 (April 1958)].

And last, a professional person will have pride in his profession and its accomplishments and live by the code of ethics of his profession. A true professional would never attempt to step into such fields as Webb suggests for the chemist or biologist in his letter, certification or no. But if the professional has the ability to teach, he will and can do a better job teaching his field than can a person with one or (in some cases) no course in that subject. A prime requisite for teaching is a great deal more knowledge of the subject matter than will ever be needed for the class. The teaching profession needs more instruction in the subjects to be taught rather than in how to teach. Certification does not make one a professional; one's viewpoint and training do.

W. W. Benton

2069 Watson Avenue,
St. Paul, Minnesota

Shutoff Pulse Illusion

The "shutoff pulse illusion" described by R. L. Ives in the 30 January issue of *Science* [**129**, 272 (1959)] is clearly the temporal analog of the well-known Mach spatial gradient ("Mach ring") effect [E. Mach, *Sitzber. Akad. Wiss. Wien, Math. Naturw. Kl. Abt. IIa* **52**, 303 (1865)]. Ives has drawn two-dimensional spatial patterns to illustrate diagrammatically the time-intensity course of the pulsed signals he used.

The direct comparability of Ives' temporal gradients with Mach's spatial gradients is borne out by the fact that if one actually stimulates the eye with two-dimensional spatial patterns of precisely the forms diagrammed by Ives, one perceives spatial brightness variations of the same kind as the perceived temporal variations described by Ives as the "shutoff pulse illusion." Similar stimulus patterns of many degrees of complexity were, as a matter of fact, designed and used by Mach to establish the empirical relations between perceived brightness and the derivative functions of the spatial distributions of light intensity. The spatial distributions used by Mach in his experiments are illustrated in his article and are reproduced in some of his other papers [*Sitzber. Akad. Wiss. Wien, Math. Naturw. Kl. Abt. IIa* **54**, 131 (1866); *Vierteljahr. Psych.* **2**, 38 (1868)]. In the same connection, it is also of interest to note that Ives' diagrammatic representation of his time stimuli and their associated perceptual effects are remarkably similar to Vivian O'Brien's analogous representations of spatial patterns that give rise to Mach rings. See Fig. 9 of O'Brien's paper on contour perception [*J. Opt. Soc. Am.* **48**, 112 (1958)].

Mach's analysis of perceptual effects of this type led to his brilliant deduction that the phenomena could be explained only by assuming mutual interactions among adjacent retinal positions —a concept which has in recent years received direct confirmation from electrophysiological studies of neural activity. See, for example, papers by Hartline [*Harvey Lectures* **37**, 39 (1941–42)] and Hartline, Wagner and Ratliff [*J. Gen. Physiol.* **39**, 651 (1956)]. These interaction effects actually serve to enhance brightness and color differences between adjacent stimuli, whether the proximity is spatial or temporal (as in Ives' example). Because of this differential enhancement these effects are basic to the fineness of visual discriminations, and hence, as Hering emphasized, are basic to veridical visual perception of both contours and temporal sequences in the everyday discriminations of boundary changes in the visual field.

Dorothea Jameson
Leo M. Hurvich

Department of Psychology,
New York University, New York

New Products

The information reported here is obtained from manufacturers and from other sources considered to be reliable, and it reflects the claims of the manufacturer or other source. Neither Science *nor the writer assumes responsibility for the accuracy of the information. A coupon for use in making inquiries concerning the items listed appears on page 1694.*

■ PULSE-HEIGHT ANALYZER accepts pulses of either sign up to a maximum rate of 1600 per second. The system's memory can be divided into either 100 or 150 channels; the energy scale may be either linear or exponential. The Hutchinson-Scarcott principle is used; information is stored in two torsional acoustic delay lines. The analyzer can subtract counts from a spectrum already in the memory. In conjunction with a live-time integrator, background count can be automatically subtracted from a spectrum. Readout facilities include an analog output for pen recorder and automatic printing in decimal form on adding-machine tape. (Marshall, Dept. 856)

■ TRANSISTOR TESTER permits measurement of the transistor beta parameter while the transistor remains in the circuit. The tester will also measure beta and collector leakage current parameters with the transistor removed from the circuit. The unit operates either from self-contained batteries or from line power. (Sierra Electronic Corporation, Dept. 871)

■ MAGNETIC TAPE RECORDER features seven channels of information with 1-Mcy/sec bandwidth. Tape width is ½ in. Tape speed is 120 in./sec, which allows 12 min of running time with standard 1-mil tape. Timing is reproducible to ± 0.005 percent. Peak flutter and wow are ± 0.1 percent or less. Starting time from rest to full speed is 4 sec. Input impedance is 93 ohm, and input voltage of 0.1 v peak-to-peak is required. Output signal level is 2 v at 93 ohm. (Minnesota Mining and Manufacturing Co., Dept. 872)

■ PARAMETRIC PREAMPLIFIER for the 350- to 500-Mcy/sec range, when coupled to a conventional ultrahigh frequency receiver, achieves over-all receiver noise figures below 1.0 db with bandwidths of approximately 1 percent. The varactor which is used as the working element of the parametric amplifier is said to be relatively insensitive to radio-frequency burnout and cross-modulation effects. (Microwave Associates, Inc., Dept. 874)

■ PRESSURE-SWITCH TRANSDUCER is capable of sensing pressure levels of from 0.5 to 4000 lb/in.^{2} by interchange of internal modular components. Eight switches will cover the entire range. Calibration is accomplished by rotation of an external pressure-setting adjust-

ment. All moving parts are sealed by O-rings in an aluminum housing. Weight is 6 oz. A mounting bracket for vibration isolation to 2000 cy/sec and 50 *g* is available. (Hayden Switch, Inc., Dept. 875)

■ DUAL-CHANNEL AMPLIFIER for voltage and current is designed for use with the manufacturer's oscilloscope. The instrument provides simultaneous measurement and observation of both a-c voltage and current waveforms. Electronic switching between channels, either by alternate sweeps or by 100-kcy/sec chopping, allows a direct comparison of voltage and current relationships within a circuit. The current channel is equipped with a current-sensing probe that is clamped around a wire. (Hewlett-Packard Company, Dept. 879)

■ PULSED OSCILLATOR provides pulse lengths continuously variable from 1.5 to 15 μsec. Durations of 30 μsec are obtainable with less than 5-percent drop. Rise and fall time are less than 0.3 μsec above 20 Mcy/sec and within 3 cy/sec at lower frequencies. Delay is provided in three overlapping ranges to 200, 1100, and 11,000 μsec. A separate delayed trigger output is provided for oscilloscope synchronization, and a gating pulse coincident with the radio-frequency output is available for blanking or intensifying. Power level is such that transmission at 1 Mcy/sec through 6 in. of air is possible with barium titanate transducers. (Arenberg Ultrasonic Laboratory, Inc., Dept. 882)

■ VIBRATION PICKUP is an eddy-current-damped unit with response constant within ± 5 percent between 40 and 2000 cy/sec and within ± 10 percent between 30 and 2000 cy/sec. Sensitivity is 96.3 mv/in. sec. The pickup will function continuously at temperatures between −85° and 500°F and will withstand continuous acceleration up to 50 *g* and intermittent acceleration up to 100 *g*. Size is 1.42 in. square by 1 in. high. (M. B. Manufacturing Co., Dept. 884)

■ DATA CAMERA records both picture and data on one film strip. Recording of the auxiliary data is accomplished through the use of split optics. The optical path for imaging the data panel containing indicating instruments passes behind the shutter so that data-recording exposure is independent of target exposure. The auxiliary data area is 3/16-in. wide and extends the height of the frame. The area for the picture is 13/16 by ¾ in. The camera generates timing pulses to actuate illumination of the data panel. (Flight Research Inc., Dept. 888)

JOSHUA STERN
National Bureau of Standards
Washington, D.C.

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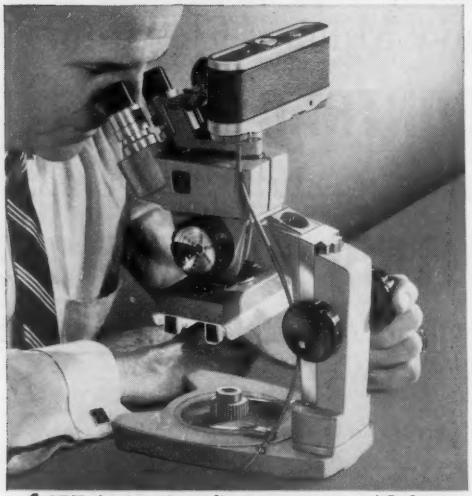

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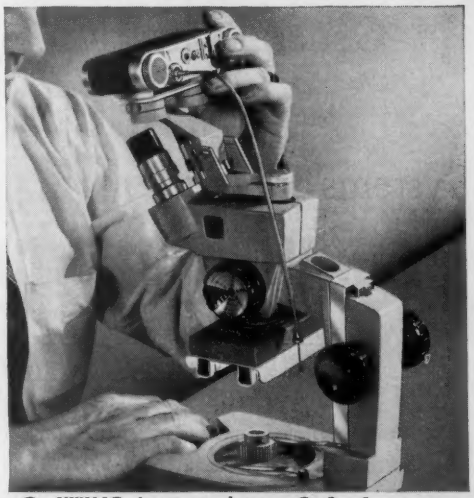

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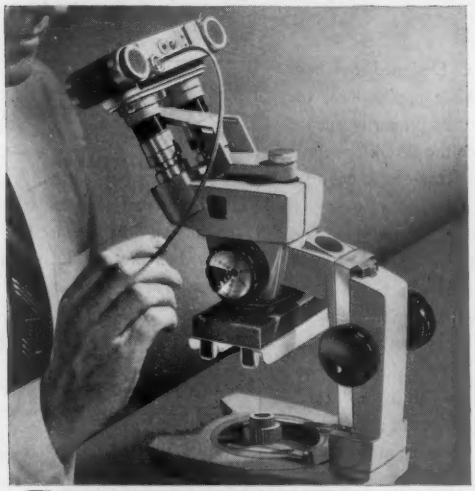

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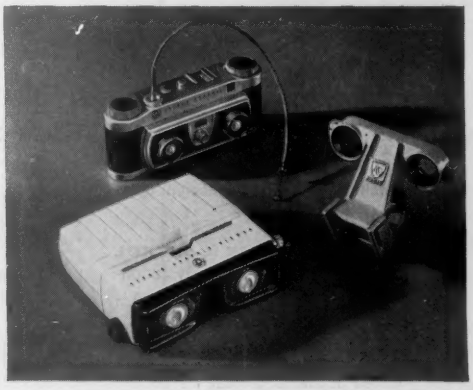

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